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THE INCIDENCE OF HEART DISEASE IN SAN FRANCISCO.

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Professor of Principles and Practice of Medicine, Cooper Medical College, and Physician to Lane Hospital.
SAN FRANCISCO.

My object in writing this paper is to throw some light on the frequency of organic heart disease in San Francisco; on the relative frequency of the various forms; and on the factors that make the frequency what it is. In order to accomplish this purpose I have drawn on two sources of information. The first of these is the records of the General Medical Clinic in the dispensary of Cooper Medical College; and the second is the autopsies performed by my colleague, Dr. William Ophüls, professor of pathology in Cooper Medical College. In the medical clinic I have had opportunity for personal investigation of the cases concerned in the preparation of this paper, and know the facts to be as stated. As regards the autopsies, they were all made by Dr. Ophüls himself, who has kindly placed his personal records at my disposal.

Some explanation must be given at the outset as to what has been included under the term "heart disease." It is so often difficult to decide that the heart is really unsound, and that the heart symptoms of which complaint is made are not, in fact, due to disease of some other organ. Every clinical investigator must have certain rules for his guidance, and it is only fair to state first of all what rules have been followed in determin-

ing the presence of heart disease in the cases herewith reported.

First.—Although it may seem superfluous to state that no case has been diagnosed on symptoms alone, yet this statement is not superfluous, because such diagnoses are sometimes made.

Second.—No case in the group reported has been diagnosed on physical signs alone, especially not by the mere presence of murmurs. Nothing is more familiar to the teacher of medicine than the certainty with which a medical student rushes from the discovery of a murmur to the conclusion that valvular disease exists; while with increasing experience the murmur itself becomes less and less important as an indication of organic disease. I would not have it suspected, therefore, that diagnoses have been made in this way among the cases collected. On the contrary, so great has been the anxiety for conservatism in diagnosis, that no cases have been set down in the records as heart disease unless besides the murmur there was definite evidence present of alteration in the area of cardiac dullness, with symptoms and signs of broken compensation, either at the time of the first examination, or previous or subsequent to it. In other words, heart disease has not been considered to exist, unless it caused some, at least, of the well-known symptoms and gave rise also to the well-known physical signs.

Third.—Cases of cardiac neurosis have been entirely excluded. The patient that comes complaining of the heart is one of the most common visitors at any dispensary clinic; but rarely are such patients found to have organic disease of the heart. Naturally among the class who apply at an out-door clinic, there are many of the victims of various forms of dissipation and excess. Poverty, ignorance and vice do not always go hand in hand, but they are extremely frequent associates in the people with whom we have to deal. The various forms of cardiac neurosis—palpitation, tachy-

cardia, heart pain, consciousness of heart action, have been observed even more frequently amongst our patients than real heart disease. But these false cases have been carefully distinguished from the true and all have been omitted in making up the list presented in this paper.

Fourth.—Still another point to be made clear is, that cases of hypertrophy or of dilatation of the heart, secondary to some other disease, have not been included in this list. For instance, in all the cases of chronic nephritis with secondary heart changes, no record has been made in this group of heart cases. Similarly with cirrhosis of the liver, pulmonary tuberculosis, the primary anemias and diabetes, no cases have been recorded as having heart disease, no matter what secondary changes were manifest in the heart. In other words, our effort has been to limit the inquiry to cases in which the heart was plainly the organ primarily diseased. The greatest difficulty has been encountered in the effort to determine the relation of arteriosclerosis to myocardial changes. Here it has been found practically impossible to decide whether one or the other process first took place, or whether they both developed simultaneously. In no case, however, has myocarditis been diagnosed without the presence of definite symptoms and physical signs referable to the heart, no matter what grade of arteriosclerosis was demonstrable in the peripheral vessels.

I. FREQUENCY OF HEART DISEASE IN SAN FRANCISCO.

After these preliminary explanations I pass to the consideration of the first question, viz.: How often does heart disease occur in San Francisco? I have looked over the records of 3,648 cases seen in the medical clinic of Cooper Medical College, during the five years from Jan. 1, 1900, to Jan. 1, 1905. Among these there occurred 135 of organic disease of the heart. Ninety-seven of these cases came to the clinic with the

symptoms and signs of broken compensation. In the other thirty-eight compensation was fair at the time of examination, but the physical signs were nevertheless definite and there was a history of broken compensation on some previous occasion. Several of the cases came to the clinic repeatedly with attacks of broken compensation occurring again and again during the five years. The percentage of heart cases was therefore 3.7, or, in other words, out of every thousand who presented themselves for all sorts of medical diseases, thirty-seven were found to have unsound hearts.

The records of autopsies by Dr. Ophüls number 640. Among these autopsies sixty-one showed organic disease of the heart. This makes a percentage of 9.5; which means that out of one thousand cases of death from all causes, ninety-five bodies showed organic disease of the heart. The marked discrepancy between the clinical figure and the pathologic figure may be explained in several different ways.

First.—It is common for people with a slight degree of organic change in the heart to have no symptom of ill health referable to these changes; and to die from some other acute illness, when systematic investigation at autopsy reveals lesions not previously suspected to exist.

Second.—Slight changes in the structure of the heart valves and heart muscle may give rise to such dubious physical signs that the clinician may not recognize their presence, even though he has sought for them.

Third.—The total number of cases is very different in the two sets of records; and if the total number were equal in each, the proportion of heart cases might be more alike.

Fourth.—It must be remembered that the cases taken from the clinic records were all ambulatory; while Dr. Ophüls' autopsies were made almost entirely upon cases that died in the City and County Hospital, or in Lane Hospital. People who go to a dispensary clinic must

of necessity be well enough to get about; but people who go to bed in a hospital, do so because they are too ill to be any longer about. Once in a hospital they are very likely to reach the pathologist, and once in the hands of a competent pathologist things are sure to be found out about them that were never known before. It is impossible, therefore, to draw any final conclusion as to the exact incidence of heart disease in this city, and as to where it lies between 37 per thousand as a minimum and 95 per thousand as a maximum. So far as I can find out, no previous attempt to establish this has been made, and this pioneer effort must of necessity give only an approximate estimate.

II. RELATIVE FREQUENCY OF THE VARIOUS FORMS.

In considering this point, a number of cases were naturally found where there appeared to be a lesion at more than one valve; but in these cases the diagnosis was always made of the lesion that seemed to predominate and to control not only the physical signs but also the clinical history. As was to be expected, the lesion most often met with was mitral regurgitation, of which there were sixty-five cases. Next in frequency came myocarditis, of which there were forty cases. While it is recognized that it is never possible to say with absolute certainty whether the myocardial change is fibroid or fatty in character, still in an overwhelming majority of the myocarditis cases there were associated changes in the vessels which spoke for fibroid change; and in only five did it seem likely that the condition present was a fatty degeneration of heart muscle. It has seemed to us that the proportion of myocardial disease to valvular disease is rather a large one, and this conviction based on clinical observation seems to be borne out by the pathologic findings in Dr. Ophüls' autopsy reports, as will presently appear. Third in order of frequency came aortic regurgitation, of which twenty-one cases were observed. All of them were typical and in two

of them that died during the time of their attendance on the clinic, autopsy confirmed the diagnosis. Finally there were observed nine cases of pure mitral stenosis. I am convinced that this number does not convey a proper idea of the frequency of this lesion; but as no patients under 12 years of age are admitted to this clinic, and as mitral stenosis is essentially a lesion of childhood, naturally the number herewith reported falls far behind the other forms. As it is, seven of the nine cases observed were in individuals under 20. No case was seen where a diagnosis of aortic stenosis could conscientiously be made.

Turning now to Dr. Ophüls' autopsy reports, out of the sixty-one cases of heart disease discovered, forty-three were cases of endocarditis and eighteen of myocarditis. As regards the orifices affected, the aortic alone was found involved eleven times; in one case no severe lesion, in three cases largely stenosis, and in seven cases insufficiency. The mitral alone was found involved ten times; in seven cases no severe lesion, in one case largely stenosis, in one case largely insufficiency, and in one case both. Both aortic and mitral valves were found involved simultaneously seventeen times. In the eighteen cases of myocarditis, fourteen showed partial obstruction of the coronary arteries by arteriosclerosis.

The observations made as regards the relative frequency of the various forms of organic heart disease are, therefore, not essentially different from those of observers elsewhere; except that there seems to be an unusual proportion amongst our cases of disease of the myocardium. This is directly attributable to the great frequency of arterial disease amongst the class of patients we meet in our clinic, a fact which accounts also, I may say in passing, for the remarkable frequency with which we observe aneurism of the aortic arch in San Francisco—a fact to which I venture to call attention at this time, without adducing statistics to corroborate the statement.

III. FACTORS INFLUENCING THE FREQUENCY.

(*A*) *Rheumatism.*—As one would expect, articular rheumatism has played a prominent part in the history of our cases who came with heart disease. Forty-nine in all had either had rheumatism at some time in their previous history, or were suffering from a subacute attack at the time of their visit. In a number of these there was the usual history of frequently recurring attacks; in others simply a history of one severe illness with a few or many joints involved. It is interesting to note the relation of rheumatism to the form of lesion present. Out of nine cases diagnosed as mitral stenosis, six had a positive history of rheumatism, usually of recurring attacks. Of the sixty-five cases of mitral regurgitation, thirty-three had an antecedent history of rheumatism. On the other hand, out of twenty-one cases of aortic regurgitation, only five had an antecedent history of rheumatism and out of the forty cases of myocarditis, only seven had ever suffered previously from rheumatism. Thus it would appear that while in San Francisco, as elsewhere, the acute infectious disease called rheumatism frequently leads to organic disease of the heart, it is the mitral valve that is most often left incapaciated, while the aortic much more frequently escapes and the myocardium suffers least frequently of all.

(*B*) *Arteriosclerosis.*—This is naturally the second great factor. It has been found present in practically all of the cases diagnosed as myocarditis, and in a large proportion of the cases of aortic regurgitation. It is recognized as a matter of course that arteriosclerosis may be manifestly present in peripheral vessels and yet, perhaps, play no part in the condition of the heart; and, on the other hand, that before changes can be discovered in peripheral vessels, advanced change may already have occurred in the coronary arteries and in the aortic arch. But two points are absolutely certain:

First.—The extreme frequency with which we observe arteriosclerosis in the clinic, as shown by thickened and hardened walls in the palpable peripheral vessels.

Second.—The fact that out of the eighteen cases of myocarditis which were found among Dr. Orphüls' autopsies, fourteen showed a greater or less degree of obstruction of the coronaries by arteriosclerosis.

Whatever the reason for it may be, degeneration of vessels is, without doubt, one of the most conspicuous pathologic conditions with which we meet in the medical clinic from which these records are taken.

(*C*) *Nationality.*—It is a significant fact that, out of the 135 cases, only forty-eight were of native stock —that is, born in the United States. What bearing this may have on the incidence of heart disease is not readily explained, but the fact remains that nearly two-thirds of our cases were of foreign birth. Nothing shows better than these statistics of a medical clinic how cosmopolitan is the population of San Francisco. Among the cases collected there were patients from Austria, Ireland, Germany, Sweden, Denmark, Italy, England, Canada, Poland, France, Switzerland, Finland, Roumania, Russia, West Indies, Belgium, Portugal, Norway, Hungary; while in the clinic, though not represented among the heart cases, we have frequent visits from Chinese and Japanese. Returning to the relation which foreign birth may bear to heart disease, the only explanation I can offer, based on my observation of these people as they come to us, is that the foreigners are afflicted not only by poverty, as all visitors at a free clinic must necessarily be, but are almost invariably filthy in their habits, addicted to the use of alcohol and tobacco, and ignorant of all proper conception of how they should live, of how they should eat, drink, work and house themselves in order to maintain health.

(*D*) *Occupation.*—It can be safely asserted that

among our cases, no one occupation has predisposed more than another to heart disease; for almost every conceivable form of labor is represented among the 135 collected here. But it must be borne in mind, on the other hand, that only the laboring class are represented in this group, and that no information whatever is given by a public clinic as to the frequency of heart disease among the prosperous, whose occupation is entirely different from that of the class from whom these cases come. It is not likely that the occupation itself has so much to do with the incidence of heart disease as has the association of any hard work with bad hygienic habits, poor food, overindulgence in alcohol and other forms of dissipation. While I have no definite statistics to offer as to the frequency of heart disease in private practice, my impression is that cases are not so frequently met with among the well-to-do as among the poor; and not so frequently among those who earn their living by their brains as among those who have to earn their daily bread by the work of their hands. Nevertheless, the rich, the idle, and the brain workers have diseases of their own, even if they apparently escape their share of heart disease.

(*E*) *Sex.*—Only thirty-five of the cases were women, while one hundred were men. While the fact that the number of males in the group so largely exceeds the females may be partly explained by the fact that the number of men presenting themselves for treatment at a dispensary clinic is always greater than the number of women, still there is no such disproportion in the attendance as there is in the number of these cases of heart disease; and the inference seems justifiable that in San Francisco, at least, heart disease is more common among men than among women.

(*F*) *Age.*—As is well known, there is no time of life exempt from heart disease, and our cases were found distributed among individuals of every age from 12 as a minimum to 81 as a maximum. During the various

decades they occurred as follows: 12 to 20, nine; 20 to 30, sixteen; 30 to 40, seventeen; 40 to 50, thirty-two; 50 to 60, twenty-nine; 60 to 70, twenty-six; 70 to 80, six. Of the nine cases under 20, seven were mitral stenosis and two mitral regurgitation; of the sixteen between 20 and 30, ten were mitral regurgitation, two were aortic regurgitation, two were mitral stenosis and two only were diagnosed as myocarditis. Of the seventeen cases between 30 and 40, ten were mitral regurgitation, five were aortic regurgitation and only two were myocarditis. Thus it will be seen that all of the cases of mitral stenosis occurred under the age of 30 and the great majority under 20; while, on the other hand, out of the forty cases in all of myocarditis, only four were observed in patients under 40. The mitral regurgitations were found quite evenly distributed throughout all the decades, almost the same number for each ten years up to 70; which would seem to indicate not only that mitral regurgitation has no predilection for any particular time of life, but also that its prognosis is better than that of the other valvular lesions. Of the aortic regurgitations only one-third occurred under the age of 40, and two-thirds between the ages of 40 and 60; which would seem to indicate the part played in the production of this lesion by arteriosclerosis. This, indeed, is the most significant fact that stands out above all others in these records—the predominance of arterial disease; and advanced years in themselves lead to heart disease only as they first lead to changes in the coronary arteries, or in the aortic arch and the valves that guard the orifice of this great vessel.

CONCLUSIONS.

1. Heart disease is a common ailment in San Francisco, as it is in all large cities.

2. Among valvular troubles, the form most commonly met with is mitral regurgitation; second comes aortic regurgitation, and, third, mitral stenosis, while aortic stenosis is undoubtedly a rare affection.

3. Myocardial disease is frequently found. The factors in its incidence are those commonly supposed to cause arteriosclerosis; and the latter condition is even more often seen than myocarditis itself.

DISCUSSION.

Dr. W. Ophüls, San Francisco, said that the number of cases examined at postmortem was rather small, and a comparatively small number for statistical purposes. He was struck with the large number of septic endocarditis cases. Nearly all of these cases were diagnosticated clinically as cases of chronic rheumatism with heart lesions and Dr. Ophüls thought that the cases of rheumatism, so-called, that lead to severe lesions of the heart valves were, in the large majority, more properly speaking cases of sepsis. How frequently these heart lesions follow in instances of rheumatism, if we want to acknowledge the existence of such a condition not due to an infection with ordinary septic bacteria, is another matter. It can not occur very frequently. So that it is presumable in the course of a disease with the clinical picture of polyarticular rheumatism, but with severe lesions of the heart valves, that the condition really is a septic one.

Dr. James J. Walsh, New York, thought, with regard to the origin of rheumatic endocarditis, that there is a definite change of opinion among medical men about to come that is worth while noting. At the present time it is generally accepted that simple, acute articular rheumatism is very frequently followed by valvular heart disease; on the other hand, it is generally acknowledged that simple, articular rheumatism does not leave any marked evidence of disease in the joints. One of the pathognomonic signs of acute articular rheumatism is that it leaves no mark after it. Whenever a chronic arthritic condition remains there is more than a suspicion that the original disease was not simple acute rheumatism, but either arthritis deformans or acute arthritis, due to some other infection beside that which produces true rheumatism. Affections of the heart valves are extremely common in septic conditions of all kinds. There is scarcely any form of microbe that gets into the circulation but will not produce an affection of these delicate structures. The heart valves are, after all, joints in the tissues, that is, they represent portions of the tissues covered by serous membranes in order that they may move over one another without friction and without adhesion. Since ordinary acute rheumatism when uncomplicated does not leave any mark on the other joints in the body, it seems probable that it also does not leave any mark on the heart; at least, not nearly in the large proportion usually stated. When there is a so-called rheumatic endocarditis it is probable that there has been some secondary affec-

tion complicating the simple rheumatic arthritis. This point of view can not but be helpful for diagnosis and prognosis.

Dr. Charles Rollins Grandy, Norfolk, Va., reported that his experience with heart disease among the negroes has been rather different. Heart disease among the negroes is very common, while acute rheumatism is seldom seen. The negroes have various other diseases which they call chronic rheumatism, but which are probably nervous affections, etc. Many cases of aortic valve murmurs or even double valve murmurs occur. There may be an aortic direct murmur, although at autopsy there will not be found any closing of the valves. Men who do heavy work have dilated hearts, hypertrophied hearts, with a leak at the mitral or other valves; these are some of the cases that come to Dr. Grandy for treatment in Norfolk. In probably the majority of them there was a strain of the valve. They were young men and Dr. Grandy was able to note the blood pressure and the arteriosclerosis.

THE EFFECTS OF THE INHALATION OF THE FUMES OF NITRIC ACID.

WITH REPORT OF CASES.

J. N. HALL, M.D., AND C. E. COOPER, M.D.
DENVER.

The Denver Fire Department was called to the office of the *Denver Post* Sept. 20, 1904, at 4 p. m. On arrival they were informed that a carboy of nitric acid had been accidentally broken in an attempt to remove the stopper with a hammer. The acid spread across the floor, coming in contact with the zinc used in etching. Sawdust was used to absorb it, and, rapidly oxidizing, burst into flame here and there, resulting in the call for the firemen. Mr. Bradt, foreman of the department, who was at work in the room, states that the fumes and smoke were not especially irritating until the portable apparatus began playing on the fire, the usual carbonic acid-producing solutions being employed.

We find by examination that the acid used contained no appreciable amount of nitrous acid and was of about 38 per cent. strength. About ten gallons of it escaped from the carboy. We believe the symptoms to have been caused by the smoke, made much more irritating and corrosive by the presence of the nitric acid and the products of its union with organic matter. Dr. E. C. Hill states that under these circumstances HNO_2 would arise from decomposition of the HNO_3, and also nitric peroxid (NO_2), and nitric oxid (NO).

Haines and Peterson[1] state that nitric oxid (NO) is

1. Text-book of Legal Medicine and Toxicology.

obtained by the deoxidation of nitric acid, by the action of this acid on metals, vegetable fibers, etc. They mention, as symptoms of acute poisoning, dyspnea, tightness of the chest, coughing, fainting, cyanosis, diarrhea and collapse. Concerning one case they state:

Blood drawn on venesection tarry, thick, black and rapidly coagulating. It is of diminished alkalinity, and on dilution becomes red and shows the oxyhemoglobin spectrum.

All of these compounds are irritating when inhaled. In view, however, of the irritant qualities of many gases inhaled in fires, in the use of disinfectants and otherwise, and the more or less similar results in most such cases, we would insist on the point that the irritation of the inhaled fumes, and not the direct chemical action, is probably the dangerous feature. Thus Dr. Hall has reported[2] a rapidly fatal case of bronchopneumonia resulting from the inhalation of smoke from burning weeds and grass, the subject being a feeble asthmatic of 61 years. In the same paper were reported cases from the inhalation of chlorin, of sulphurous acid, and of formaldehyd, differing only in degree from the cases we are now studying, and from each other. The chemical effect is apparently subsidiary to the irritant one in all; but, in general, we must conclude that smoke, which is not much feared by firemen, is vastly more irritating and, therefore, dangerous when contaminated with fumes of various chemicals.

Eighteen firemen and two men employed in the office were affected severely enough to demand medical aid. Of these, four died, two on the second day, from the direct consequences, and two several weeks later from relapse. The immediate symptoms complained of while exposed to the fumes were, in order of frequency, as follows: Dyspnea, pain in the stomach, pain in the chest, headache, dryness of the throat, coughing, vomiting, dizziness, difficulty in walking, and dryness of

2. Phila. Med. Journal, 1902. "Bronchitis and Bronchopneumonia from Inhalation of Irritants."

the nose. No unconsciousness was noted. Nearly all the firemen returned to their respective firehouses, not considering themselves seriously sick. After a few hours many of them sought medical aid, and within twenty-four hours all of them excepting one were patients in the Emergency Hospital.

We next present a list of the prominent symptoms noted in 15 of the 16 cases which recovered: Dyspnea, present in 100 per cent.; cough, present in 93 per cent.; pain, present in 87 per cent., especially in the sides of the chest, stomach, lungs, throat, loins and head; dizziness and nausea, present in 73 per cent.; cough of especial violence, present in 67 per cent.; vomiting, present in 53 per cent.

During the first week of illness dyspnea persisted in 100 per cent. of the cases; 93 per cent. were confined to bed during this time. Pain persisted in all those who complained of it during the first day, and in practically the same localities.

Marked prostration was present in 87 per cent. Fever in 80 per cent., generally of moderate severity. The cough generally persisted, with bloody expectoration, in 27 per cent., and voluminous expectoration in 60 per cent. The taste of nitric acid in the expectoration was complained of by several patients.

Within the first half of the second week many of them were discharged, the average time in bed for the whole number being eleven days. Ninety-three per cent. complained of general weakness, and but one felt well on arising.

Relapse occurred in 33 per cent. of these cases, generally in the third week, and averaging 15½ days in duration. The symptoms were those of the original attack, but of less intensity.

The length of time from the exposure until practical recovery in eight cases averaged 113 days, the maximum being 210 days, the minimum 90 days. Five state that they are not well yet, and two failed to answer.

Those having any remaining symptoms nine months after the attack number eleven, or 74 per cent. These symptoms, in order of frequency, are dyspnea, "nervousness," stomach troubles of various kinds, cough, dryness of throat and nose, pain in the chest, loss of weight, dyspnea on inhalation of smoke, dizziness, pain in the loins, and headache.

There was a loss of weight in 87 per cent. of the men, entirely regained in 40 per cent., not regained in 13 per cent., and no reply was made in 47 per cent. The average loss was 25 pounds, maximum 40 pounds, minimum 20 pounds. The average regained was 18½ pounds, maximum 30 pounds, minimum 5 pounds.

Sixty per cent. find they are more susceptible to cold now than previously. The dryness of the nose is thought to be due to a beginning chronic rhinitis, due to the irritation of the fumes inhaled. The dyspnea on inhalation of smoke may well be largely nervous in origin, but doubtless in part because of the increased susceptibility of the bronchial mucous membrane due to the action of irritants. The pains in the sides of the chest are, we believe, pleuritic in origin. They were exceedingly severe in some of the cases in the first days of the illness, indicating at that time a dry pleurisy, since friction sounds were heard. The later pains may well have been sequential to such a pleurisy. The rapidity with which the pain developed in some cases suggests the likelihood of its having arisen from direct irritation of the lung by the acrid smoke.

Albumin was noted in at least one of the cases, but evidently no such damage was done to the kidneys as in some cases we have seen in which acute nephritis followed the swallowing of mineral acids. Probably little of the acid was absorbed, most of the damage from it being caused by its irritant effect.

Two of the cases died on the second day, one on the twenty-second day during a relapse, and one at the end of one month, also during a relapse.

The two who died on the second day were affected about as were those who recovered, but more severely. Cough was not a notable symptom. Cyanosis, nausea, diaphragmatic pain, dyspnea and vomiting were noted early. In both there was unconsciousness for several hours before death, and the physical signs of a progressive bronchopneumonia, but without the fever and other constitutional symptoms of an infectious disease. One of these had an extremely rapid pulse. Both expectorated frothy, blood-tinged serous fluid for some hours before death. Dr. P. V. Carlin informs us that pneumothorax developed in one of them.

The two who died during relapse suffered about as the others did during the primary attacks. Both were comparatively well during the interval. Both were exposed to cold and almost immediately entered the relapse. The two cases were similar enough so that the following description may well answer for both:

The sputum was blood streaked, thin and abundant. The cough was at times violent. Pleuritic pain was severe (and in one severe pain existed in the pharynx, larynx and esophagus). Large and small râles were abundant, at first in the lower portion of the chest, and gradually extending upward. There was moderate rise in temperature, pulse and respiration. The cyanosis was intense (and not relieved by oxygen in one of the cases, although somewhat so in the other). Both died with all of the symptoms and signs of a desperate bronchopneumonia.

Before the relapse both of the men had been discharged from the hospital as recovered from the acute condition, although both complained of moderate exhaustion, such as is common to the period of convalescence from any acute illness.

In one of them examined the day before the relapse, no physical signs of disease were found. We believe that exposure to cold, which occurred in both cases, was the exciting cause of a renewed and virulent inflamma-

tion, rapidly extending into a definite bronchopneumonia, as above described.

On two patients autopsies were held, unfortunately unknown to either of us. We quote portions of the reports to the coroner by Dr. W. S. Holmquist and Dr. H. R. McGraw:

Dolloff.—"The pericardium showed spots of metallic luster on the upper surface. The heart was filled with extremely dark coagulated blood, less consistent than clotted blood. Pleurse free. Lungs large and voluminous, on section bled freely. Some spots were devoid of air. Bronchioles filled with bloody fluid. Much of the lung tissue was edematous and heavy. Mucosa of bronchi perceptibly thickened."

"*Diagnosis.*—Deceased died from asphyxia, due to an acute congestion of the lungs; and a pathologic change in the hemoglobin of the blood."

Eyman.—(Died in relapse, one month from exposure.) The essential features are stated by Dr. H. R. McGraw "to have been those of a bronchopneumonia, with almost complete solidification of lung in places. Sections from these solidified portions showed superficial coagulation necrosis and the alveoli were found filled with necrosed cells in places. Other parts showed a beginning fibrous development. Deposits of blood pigment were noted in spots upon the peritoneum. Dilatation and hypertrophy of the heart. No changes were noted in other organs."

The pathology, in our opinion, is a combination of purely local and general effects. Locally, the inhalation of the nitrous and nitric oxids, the products of combustion, and of the chemical reactions between the acid, zinc, and the chemical solution used to extinguish the blaze, assisted by the violent respiratory efforts occasioned by the physical exertion, produced an irritation and probably a mild coagulation necrosis of the mucous membrane of the air passages and the alveoli. In the two cases that died early there was produced promptly a severe bronchopneumonia. In those dying during a relapse the necrotic areas were largely cleared up by absorption and exfoliation, leaving exposed a delicate and susceptible membrane. The exposure to cold was sufficient to excite a bronchopneumonia of especial intensity on this account, proving rapidly fatal. Dr. Hall

has reported[3] a case of lobar pneumonia in which, twenty-three days after recovery, a robust young man was exposed for a few hours to severe cold (about 20 degrees below zero), and died in a few hours of acute pulmonic congestion. It is probable that the fatal result in this case, as in those we are studying, was due to a bronchopneumonia, with great accompanying edema.

The cyanosis in the severe cases was extreme. It was doubtless in part purely mechanical, as in ordinary bronchopneumonia, but largely due to the changes produced in the hemoglobin to which we have referred, and which interfered with its oxygen-carrying capacity. We await anxiously the careful investigations of Drs. Holmquist and Edson on this feature of the cases which they have studied.

The treatment generally followed, we believe, was that of an ordinary severe bronchopneumonia. Oxygen was used in all of the severe cases, with differing but generally unsatisfactory results. In a severe case of Dr. Cooper's, aconite in minim dosage, with vigorous external counter-irritation, was followed by marked relief. This was the patient who finally died in the relapse on the twenty-second day, these measures proving ineffectual at this time.

To us it seems that the one most important factor in determining the question of death or recovery was the severity of the initial exposure. Theoretically, the inhalation of ammonia at the time of exposure should be of benefit, but this would hardly be practicable. We believe that, at present, stimulation, the use of oxygen when indicated, atropia for the edematous exudation, vigorous counter-irritation, with eliminative and supportive measures offer us the most hope in the primary attack. If recovery occurs, we would strongly urge suspension from work, rigorous avoidance of exposure, and residence for some months in a warm, equable climate,

3. Denver Medical Times, 1898.

such as one would choose for a feeble patient with chronic bronchitis. Those of the Denver cases who were able to follow such a course are at present working, and without serious symptoms. In view of the lessened pulmonary resistance, we would suggest also the adoption of effective measures for the avoidance of infection by the bacillus of tuberculosis.

If we can not save all of those exposed in the performance of their perilous duties to the inhalation of dangerous gases, we should insist the more strongly on the avoidance of anything tending to bring about relapse, which we have noted to be so fatal.[4] It is likely that we can save more lives by strict attention to this feature than by any other single measure.

We are under especial obligations to Dr. W. H. Sharpley, Health Commissioner of the City and County of Denver, for his encouragement and assistance in the preparation of this paper; to the Denver Fire Department, and to the physicians who attended other cases than those which we saw, who have so generously given us their aid.

DISCUSSION.

Dr. N. H. Neilson, Milwaukee, Wis., reported having the same experience in Milwaukee, two years ago, showing the effects of the fumes of nitric acid by inhalation. The men who were engaged in putting out the fire returned to the station house, and within one or two hours—six or seven hours after the exposure—they began to have symptoms of pulmonary congestion, as described in the paper. Some of the men died and some recovered for a time, but had relapses. Some had a chronic bronchitis and were sent to Texas, where they recovered—all but one, who became despondent and committed suicide. In these cases it was believed that the pulmonary edema was the result of the local irritation on the mucosa and not a systemic effect. Whatever systemic effect there was was from the inflammation alone. Dr. Neilson did not think that a report of the cases was published.

Dr. John H. Musser, Philadelphia, said that the autopsy

4. In the case of a fireman, quoted by Dr. Hall in the abovementioned article as dying from inhalation of smoke containing fumes of some undetermined acid, the death was also during relapse, being directly caused by pulmonary embolism from a phlebitis of the leg, at the end of the fifth week.

findings in such cases do not support the belief in the presence of any pleuritis, and he, therefore, asked as to the occurrence of the inflammation and the vomiting.

Dr. G. W McCaskey, Fort Wayne, Ind., thought that the symptoms in these cases indicate a degree of exhaustion unusual with a simple irritative bronchitis, and that the evidence points toward a severe toxemia as a result of absorption of the poisonous gases. It is peculiarly the function of the respiratory tract to absorb gases, and it seems only reasonable to suppose that such absorption would take place and should be considered in accounting for the very severe constitutional symptoms manifested by these cases.

Dr. J. N. Hall, Denver, remarked that it was rather difficut to report these cases with any degree of accuracy, because they fell into the hands of about twenty physicians. Dr. Cooper took care of six and Dr. Hall three. A pleuritic friction was well marked, beginning within twenty-four hours. Necropsies were made by the coroner's physician, and the bodies were buried before Dr. Hall knew of the deaths. He, therefore, had no opportunity to study the pathology. The toxemia was similar to what would be expected from inhalation of chlorin, formaldehyd or smoke from burning grass, but no case pointed definitely to a toxemia from the acid itself. Dr. Hall could not explain the vomiting. Although none of those exposed were supposed to be sick enough to keep in, at the end of twenty-four hours they came back to the hospital.

AFFECTIONS OF THE THYROID IN CALIFORNIA.

HERBERT C. MOFFITT, M.D.
SAN FRANCISCO.

Six years of hospital and private work in San Francisco have strengthened the conviction that affections of the thyroid, like aneurisms and early arteriosclerosis, are more common here than in many other cities of the United States. With this idea in view, letters were sent during the last months to men in each county of the state asking for information as to the occurrence of goiter, myxedema, sporadic cretinism, and exophthalmic goiter in their districts. My obligations are here expressed to many colleagues who have kindly sent reports. There seems to-day little need for review of reasons in grouping exophthalmic goiter with thyroid affections—the influence of nervous factors can not be denied the possible influence of other internal secretions in etiology is recognized, but the gland plays a chief rôle in symptomatology (even though, as Moebius says, there may be a prethyroid stage of the disease). Despite the vast amount of work of late on the parathyroids by Gley, Edmunds, Welch, Benjamins, Jeandelizo, Moussu, Vassale and Generali, Lusena, MacCallum, Brissaud, Pineles and others, it is not yet possible to say that they color in any way the picture.

The statement of Hirsch that "our information on the endemic occurrence of goiter in North America belongs for the most part to the early years of this century and is very fragmentary" can be modified in light

of articles by Richardson, by Adami on goiter in Canada, by Osler on "Sporadic Cretinism in America," by Dock on "Goiter in Michigan." *The Medical Sentinel,* February, 1904, had an editorial on goiter in the northern Pacific states, and lately Musgrave of Washington described the great frequency of the condition in the Wenatchie and Puyallup Valleys in animals as well as man. Praslow years ago reported cases of cretinism among Indians near Cape Mendicino, Humboldt County, and among the Spaniards in Southern California. Osler in his article on sporadic cretinism wrote: "Praslow's account of the occurrence of cretins in California I have not seen, but I have letters from several correspondents in that state who know nothing of its existence at present, while in the State Insane Asylum at Stockton, Dr. Hoisholt tells me there are only two cases." It is interesting to note from reports of Dr. Gross of Eureka and Dr. Delamere of Ferndale that goiter is common in Humboldt County, not far from Cape Mendicino, although accounts of only two cretins are sent from that district. I have seen two cretins among Indians near Kelseyville, Lake County. Reports from Southern California do not substantiate the account of cretinism among the Spanish settlers.

GOITER.

Data concerning goiter must of necessity be unsatisfactory, as slight or even moderate enlargements of the gland are often overlooked; and, as in all statistics, the personal equation of the reporter must be considered. A few weeks since a physician came personally to report the absence of thyroid affections in his district and presented himself a good example of myxedema. The testimony of physicians from counties about San Francisco Bay (Marin, Alameda, Santa Clara, San Mateo, and San Francisco), confirms the idea that moderate enlargements of the thyroid are common. Most patients are natives of California, and inheritance from

parents coming from endemic goiter regions of Europe would seem to play little part. Dr. Eleanor Bancroft, Berkeley, writes me that 5 per cent. of the young women entering the University of California in 1904 had enlarged thyroids. Since January 1, 1905, I have noted moderate enlargement in 75, large goiters in 8 patients out of 546; 14 cases were in men. This would give a percentage of 15.2 in individuals, nearly all of whom are native born, or who have lived for years in California. In one family five members have goiter, in another three. In a number of young women accompanying nervous symptoms seem definitely referable to thyroidism, but in the majority of instances the enlargement is without influence on the general condition.

Dr. Pope of Watsonville has noticed 12 decided goiters in 1,200 cases, but writes that small tumors are much more frequent. Reports from the southern part of the state (San Diego, Riverside, San Bernardino, Los Angeles, Santa Barbara, Kern, Tulare, Kings, and San Luis Obispo counties) would indicate that goiter is less common there than in the bay counties. Dr. von Zwalenberg of Riverside says it is much less common than in Michigan. Dr. Sanborn writes from Redlands that there are about 40 cases of moderate goiter in the practice of different physicians there. Los Angeles and Pasadena physicians report the condition uncommon, and men from Fresno, Tulare and San Luis Obispo as rare. Through the kindness of Dr. P. K. Brown, however, I am able to quote a letter from Miss Jacobs of the Los Angeles Normal School in which she says goiter is common in the young women in attendance, and that not a few report other cases in the family—one term 8 per cent. had enlargement of the thyroid.

The interior mountain counties of the central part of the state seem much less affected. Letters from Madera, Merced, Mariposa, Stanislaus, Tuolumne, Amador, El Dorado, Placer, Nevada, Sierra, Butte,

Yuba, Sutter, Yolo, Colusa, San Joaquin report few cases. Dr. W. A. Briggs thinks moderate sized goiter fairly common in Sacramento county. Dr. Dempsey of Vallejo, Solano county, sees enlarged thyroid in 4 per cent. of his patients. Lake, Napa and Sonoma have few cases. Dr. Margaret Evans mentions a family in Calistoga, Napa county, four members of which have goiter. Of the northern coast counties Mendicino and especially Humboldt appear to show endemic goiter. Dr. Bond of Ukiah writes: "I can only state in a general way that thyroid enlargement is very prevalent in this vicinity, most cases being of American parentage and without symptoms. Dr. H. G. Gross of Eureka writes that he sees a number of cases practically all of which come from an area about ten miles long and three wide, partly in the valley and partly in the foothills. Dr. H. S. Delamere of Ferndale, within the district spoken of by Dr. Gross, says: "Thyroid enlargement is quite prevalent here." Dr. Jorgensen of Fortuna, Humboldt county, however, sees but few cases. Professor A. C. Lawson of the University of California, in a paper on "The Geomorphogeny of the Coast of Northern California," describes the peculiar formation known locally as the "Wild-Cat Series" that extends through Humboldt county. Its peculiarity depends on the softness of the beds in general, the frequent alternation of harder and softer rocks, and the deep erosion of the Eel River and its tributaries. It would be of interest to map out the goiter region with reference to this peculiar terrane. The entire peneplain consists of marine deposits, pliocene and postpliocene, with a coastal strip of later mesozoic and tertiary rocks. The reports deal but slightly with questions of etiology—mention is made simply that most cases are seen in women and that enlargement of the neck has often been first noted during pregnancy. In several instances note is made that the goiter has enlarged with each pregnancy. No mention is made of

goiter in animals, but I have seen it in one horse and two dogs in the past year.

MYXEDEMA.

Reports here are less equivocal. The bay counties again show the greatest number of cases partly on account of greater population, and partly because cases from a distance drift to San Francisco as a center. I have descriptions of 30 cases throughout the state. Tehama, Monterey, Sacramento, Santa Barbara, Riverside, Stanislaus, Marin, Yuba, Mendicino, Santa Cruz, Yolo, Kern and Colusa report one case each; Solano, Santa Clara, Butte, two cases; Fresno and Los Angeles three, and Alameda sends five. San Francisco physicians send accounts of 43 cases, without duplicating any of the reports from other counties as far as can be ascertained. Adding 10 of my own, there is a total of 53 cases from San Francisco, and 83 throughout the state. I have purposely omitted reports of doubtful cases, accounts of *formes frustes,* or descriptions of exophthalmic goiter with myxedema. In 50 cases in which mention was made of sex, 39 were women and 11 men. Age varied from 18 to 64. Thirteen had decidedly large thyroids, the myxedema resulting from changes in old goiters. In 22 the thyroid was not palpable, and no mention of the gland is made in 31. Of 55 ten were of foreign birth, but had been years in California. Twice the condition resulted from operation on goiter. Two of my cases were born in Norway. Two had spent some years in Alaska, and symptoms developed while there. Emphasis in description is laid chiefly on skin, voice, and mental changes and disturbances in locomotion. Three women had frequent epileptiform attacks which did not yield to thyroid medication, although skin and mental conditions improved. A woman reported by Dr. P. K. Brown had profuse menorrhagia before thyroid treatment was begun.

Some years ago I saw myxedema in a girl of 20

whose mother had just died of the disease. Skin of the face and over the extensor surface of the arms was thick and dry, there was a diffuse growth of hair over the face and arms that had appeared during the last year; the voice was remarkably deep and harsh, menstruation had ceased ten months. The fundus showed atrophy of the nasal side of both discs, and color vision was limited in the temporal half of both fields. In all probability change in the hypophysis was the cause of eye symptoms and perhaps of the hypertrichosis. Menstruation appeared under thyroid extract and the skin grew better, but the girl committed suicide and no autopsy was obtained. Uhthoff described blindness in a boy of 6 with myxedema; vision improved under thyroid, and this was attributed to shrinking of the hypophysis. Coppez describes retrobulbar neuritis from thyroid feeding, but no instance has fallen under my observation. Endeavor has been made chiefly by Brissaud, Murray and Pineles to distinguish between myxedema of thyroid and of mixed thyroid and parathyroid origin. They would attribute considerable influence to the parathyroids in determining sexual and mental changes. In cases with profound mental changes, therefore, we would look more closely for other signs of disturbed parathyroid function—particularly for evidence of tetany or convulsive seizures. Only one of my cases was mentally profoundly affected, and here the Chvostek and Trousseau phenomena were constantly absent. In one woman with most marked exophthalmic goiter and epileptiform attacks the Chvostek phenomenon was present on two examinations; partial thyroidectomy led to disappearance of all symptoms, no tetany developed, and the patient has been well three years.

FORMES FRUSTES.

Very interesting to me are the *formes frustes.* I have notes of 11 cases, 5 men and 6 women, all of whom presented the same clinical picture, and in whom definite

improvement took place under thyroid medication. One was a woman of 35, two were men of about 45, and the others were from 55 to 65; the sister and daughter of one woman had goiter; one man and two women had small goiters. Such cases are fairly common in the literature of thyroid insufficiency. Some of these people have for years had dry skins, thin hair, pains between the shoulders, paresthesiæ, joint pains. In two of my cases influenza seemed a factor in precipitating thyroid symptoms—skin changes, nervous unrest and tachycardia. Most characteristic is the dry skin, scaling of the scalp, thinning of the outer half of the eyebrows, loss of hair on the neck and in the axillæ. Fat pads occur above the clavicles, and not infrequently there is a large pad over the upper dorsal vertebræ, a bib-like roll across the neck and upper sternum, thickening of the subcutaneous tissue across the lower ribs and above the elbows and knees on the extensor surface. Pains in the knees and ankles and occasional "giving away of the legs" are frequent. The voice has often a peculiar deadened husky quality.

Five instances of infantilism of the thyroid type described in detail by Brissaud, Meige, Hertoghe and others have come to my notice in the past two years. Two boys of 14 and 18 grew quickly under thyroid treatment, and showed increased development of pubic and axillary hair and of genitalia. One boy of 17 was excessively fat and had complications of muscle dystrophy and coxa vara. Another boy of 16 died of diabetes; thyroid extract had no effect on the sugar elimination. The fifth boy had acute nephritis and uremic convulsions.

SPORADIC CRETINISM.

In Osler's article on "Sporadic Cretinism in America" are included three cases from California, two of Dr. Hoisholt from the Stockton Asylum and one of Dr. Osborne from the Home for Feeble-minded Children at Glen Ellen. I have reports outside of San Francisco of

37 cases that from descriptions or photographs seem definitely examples of cretinism. Mongolian idiots and chondrodystrophy cases are not included in the classification. Of these, seven were born outside of the state in Mexico, Wisconsin, Illinois, New Zealand, New York, New England, and four have died. Doubtless the list can be extended by a more thorough canvass at some later day. Dr. Dawson, superintendent of the Home for Feeble-minded Children at Glen Ellen, Sonoma County, writes that there are several cases of idiocy of Mongolian type and a few cretins, but these are not included in the above. Physicians in San Francisco send me accounts of 28 cases, to which I can add 7 of my own, making a total of 61 cretins now living in the state, and all native born. The majority of reports chronicle absence of palpable thyroid enlargement. No valuable data as to etiology are available. Dr. Frances Sprague reports a girl of 2 from the Children's Hospital in San Francisco who died of general tuberculosis, with extensive tubercular changes of the thyroid. Dr. Millicent Cosgrave sends me notes of a girl of 5, born in New York. Mother and grandmother had goiter, and the maternal grandfather died of tuberculosis. The child seemed normal during the first year, and walked at 18 months, at 3 had measles and later tuberculosis of the glands of the neck. Since then she has not walked well, has backache, is nervous, skin dry and rough, appearance that of a cretin, is extremely stupid, abnormally developed—is as tall as a child of 10. Breasts, hips and limbs look like those of a girl of 16. The mental condition has improved under thyroid treatment. Brissaud calls attention to tuberculosis of the cervical glands as a cause of myxedema. In one of my cases symptoms developed soon after diphtheria. Dr. Dempsey of Vallejo reports seeing a cretin whose mother had a large goiter, with myxedema. Dr. Sprague mentions a girl of 14 with a big thyroid, another of her cases was but 18 months old. In a case of mine—a

girl of 7—the parents were from the south of France. From the history, the father's sister was probably a cretin, and a brother of the patient died at 6 months in a condition suggesting cretinism. Dr. P. K. Brown tells me of two brothers born in San Francisco whose parents are German and perfectly well. In the greatest number of cases parents were born in California. In three instances parents were from the Azores, in two from Austria, in two from southern Italy, in three from Ireland. Detailed descriptions will be left to a later paper, but photographs of ten cases are now available.

EXOPHTHALMIC GOITER.

This affection would appear to be much more common in the counties about San Francisco Bay than in the other parts of the state. Dr. Emmet Rixford of San Francisco sends me notes of 8 primary cases and 3 secondary to goiter of years standing; Dr. T. W. Huntington, 5 primary and 8 secondary; Dr. W. I. Terry, 10 primary; Dr. J. H. Barbat, 10; Dr. Mac Monagle, 29. Physicians content themselves, as a rule, with saying that the affection is "common" or "decidedly frequent." Dr. Abrams has seen 30 cases. My own list includes 33 well marked cases of exophthalmic goiter, excluding *formes frustes.* Of these, 9 were male and 24 female; 7 occurred in patients with goiters of years' standing. Most observers agree as to the thyroid factor in the disease, but emphasize the influence of an unstable nervous system and the immediate effect of nervous shock. Dr. J. H. Barbat saw 3 cases develop acutely after fright. Some few years ago in the wards of Dr. Kerr in the City and County Hospital of San Francisco I saw an Italian with unusual history. Three weeks before, in perfect health, he had been out prospecting in one of the interior counties, had strayed off, and was lost in the mountains for two days. He was sick from that time, excited, restless, could not sleep, vomited, grew rapidly thin, had breath-

lessness, palpitation, trembling, could scarcely walk. Examination showed exophthalmic goiter, with cardinal signs, emaciation, terrifying unrest. For days he remained the incarnation of terror, but then slowly changed to the more uneventful stage of the disease.

In a woman under the care of Dr. Abrams, the father and brother showed symptoms of the disease. Two of my patients were mother and son and two brother and sister. The mother of one young woman under my care has myxedema. Dr. Crowley of Oakland reports exophthalmic goiter in mother and son. Dr. F. L. Adams of Oakland reports the disease in mother and daughter; the mother is from Derbyshire, a well-known center for goiter. Another of his cases gives history of the same affection in her mother and mother's mother.

In the reports of simple goiter, frequent mention is made of associated nervous symptoms, tachycardia, and tremor. These cases are similar to the ones described by Mikulicz and Rehnbach, by Kocher and others as instances of thyroidism associated with goiters of varying types. They form a transition to true exophthalmic goiter developing in individuals who for years have had goiter without symptoms. In a woman of 41, seen two years ago, there had been a marked goiter for 18 years; eight years before nervous symptoms became bothersome; there was exophthalmos, tachycardia, tremor. Swelling of the eyelids and a peculiar brawny infiltration of the side of the neck and face led to a diagnosis of complicating kidney disease, but this was not present. The swellings were analogous to the hardening of the skin of the face reported by J. Schulze, a firm infiltration not like true scleroderma nor yet of the consistency of myxedema. In a woman seen four years since, there had been a moderate goiter for years. During pregnancy signs of myxedema, as thinning of the hair, dry skin, supraclavicular pads, were reported to have developed and to have disappeared under thyroid extract. Unfortunately with continuance of

the thyroid extract a typical exophthalmic goiter developed, which was marked by all cardinal signs when I saw her.

Breuer of Vienna and Gautier of Geneva have lately emphasized anew the occurrence of exophthalmic goiter after treating goiter with iodin preparations. Breuer cited a case developing after the use of K I—a syphilitic woman who had shown no previous struma. Rilliet, 1860, and Lebert, 1862, gave many instances of iodism in goiter cases. Theodor Kocher, in a recent article on "Die Therapie des Kropfes" in the *Deutsche Klinik,* gives a masterly review of the action and dangers of iodin compounds. His conclusions are based, in part, on the studies of iodin elimination in normal individuals and cases of goiter by A. Kocher published in vol. xiv of *Die Grenzgebieten der Medizin und Chirurgie.* He makes clear that most symptoms are due to thyroidism rather than iodism. With quick recession of a goiter, danger of intoxication greatly increases, but the disappearance of a struma is not necessary for production of symptoms. The smallest dose of K I may cause severe thyroidism in exophthalmic goiter or cause rapid emaciation in the newborn or in pregnant women. "In excited, unduly animated, thin individuals who always have congested faces, who tremble at nothing, get palpitation on the least occasion, and who sweat easily, one has to deal with beginning thyroidism, and one may cause outspoken exophthalmic goiter through careless use of iodin."

I have had several cases of iodism after small doses of K I in patients with small goiters, and now make it a rule to examine the thyroid and to look for signs of exophthalmic goiter before prescribing it. In one young man in whom K I, syr. acid. hydriod. and tr. iodi gave toxic symptoms, iodipin was given hypodermically with impunity, confirming the observations of Schuster and Lesser; it could be demonstrated in the tissues by *x*-ray plates six weeks after injection. According to Gautier,

the source of plant and water iodin supply is the iodin "dust" given to the atmosphere by sea water. Rilliet of Geneva thought a change to the seashore might develop symptoms of exophthalmic goiter in patients with struma. It is an interesting speculation whether the number of cases about San Francisco are in any way due to the prevailing strong sea winds. It is certain that a few cases from the interior have done worse on the coast, and insomnia is apt to be a bothersome feature of the change. In eight of the reported cases there is noted a combination of exophthalmic goiter with myxedema, but description lacks sufficient detail to admit such classification. It is well known that edema and skin infiltration of different kinds may occur in pure exophthalmic goiter. Kocher describes a number of such cases. Dr. Rixford reported a remarkable case of a young woman of 29, who was married a few weeks before contracting scarlatina. Three months later a goiter, the size of a walnut, was observed. One year later there was rapid growth during pregnancy, and still greater enlargement after a second pregnancy two years later. General edema, tremor and choreic movements were noted, besides the usual symptoms. Edema rapidly disappeared after operation. In two of my cases, fat pads and hard infiltration of the skin over the lower ribs persisted after operation. In a discussion on "Internal Secretions" two years ago (reported in the *Clinical Journal*), Horsley described certain anomalous cases of myxedema, with a peculiar excitable mental state, inability to exert, symptoms of heart insufficiency, and fat pads or diffuse skin infiltration. He regarded them as combinations of athyroidism, with a certain amount of aberrant internal secretion, the "dysthyroidism" of Moebius. He advises in treatment almost total removal of the gland, and then supplementing its secretion with thyroid extract. I have under observation for two years and a half a woman who lived abroad years ago, for some time in

centers of goiter, such as Geneva and the Pyrenees, and who for years had the nervous and heart symptoms of exophthalmic goiter. There has never been exophthalmos, but at times there is a fixed stare or glare that to me is rather characteristic. For six months the pulse was never below 100, and during attacks of palpitation 160 or more. There are at times remarkably large supraclavicular pads, such as are seen in myxedema, and a diffuse bib-like pad of the same tissue, feeling like half solidified fat, stretches across the front of the neck and down irregularly four or six inches below the clavicles and across the sternum. An apron of the same kind extends across the epigastrium and lower ribs. The case is similar to those reported by Horsley. Of chief interest is the variation of the condition under alternate treatment with rodagen and iodid of iron as described below.

Formes frustes of exophthalmic goiter would require a separate paper. There is danger in labeling too many indefinite nervous affections with this convenient diagnosis, which only a combination with cardinal symptoms should justify. I have seen enlargement of the thyroid, with nervous symptoms and tachycardia, the result of masturbation in young men. Since my attention was called to it by Ortner of Vienna, I have seen the same thing, the result of excessive tobacco smoking in boys. Of interest in considering eye symptoms of the disease are the reports of Arslau, Spiegler, and Holz concerning the occurrence of exophthalmos in adenoid cases and its disappearance after operation. During the last year Dr. C. M. Cooper and I have been testing the value of von Graefe's sign in diagnosis. It was curious to note the occasional development of this and Stellwag, with other symptoms of mild thyroidism, after administration of K I. Our results confirm the observations of Sharkey and of Flatau that the sign is frequently seen apart from thyroid disease. It was particularly com-

mon in Italians, probably because of the greater tendency to keep the eyes widely open while talking.

THERAPY.

The goiters seen here rarely demand operation on account of their size. Dr. Rixford, Dr. Terry, Dr. Rosenstirn, however, send me accounts of 20 operations for cystic or adenomatous goiter. The necessity of caution in the treatment of goiter, and particularly exophthalmic goiter, with iodin compounds or thyroid extract has been sufficiently emphasized above; the senseless administration of thyroid extract in large doses for obesity, arteriosclerosis, and other cases of supposed thyroid insufficiency should be discountenanced. Cunningham has attempted to prove that toxic symptoms are due to contaminating cadaveric derivatives and not to the active thyroid principle, and claimed that fresh glands may be given with impunity in exophthalmic goiter. The occurrence of well-marked exophthalmic goiter after administration of K I or iodothyrin in goiter cases would, however, speak decidedly for the theory of hyperthyroidization.

The reports of treatment in myxedema and cretinism are enthusiastic. It is usually not necessary to give large doses of a good thyroid preparation; in cretinism I begin with one grain daily and rarely go beyond 5 grains. Many myxedema patients need only small doses, even at first; some of them can not take more than 2 or 3 grains without disagreeable nervous symptoms. Dr. Ebright tells me of a man of 64 who had severe rheumatoid pains each time the dose was increased beyond two or three grains daily. Bramwell speaks of an acquired intolerance, and mentions a case in which large doses were well borne, but later even 1/20 of a tablet produced marked toxic symptoms. Paresthesiæ and other unpleasant symptoms may be modified by giving Fowler's solution at the same time. Opinions are in accord that preparations representing the whole gland can not wholly be

replaced by the active principle iodothyrin. Bramwell, Magnus-Levy, Warner von Jaurenegg report encouraging results in the treatment of endemic as well as sporadic cretinism.

Until recently medical treatment of exophthalmic goiter was limited to electricity, hygienic measures, and a long list of drugs for symptomatic use. It is very difficult to judge of the efficacy of any method of treatment in an affection notoriously so uncertain in course and symptoms. I have seen good results from long-continued faradism, as recommended again of late by Horsley, the patients use the battery themselves for an hour or two daily, fastening the electrodes over the neck, front and back. With the treatment suggested by Wm. Thompson, I have seen no effect in marked cases. Strontium or calcium bromid—30 to 45 grains daily—or the bromid of quinin, 15 to 30 grains daily, as recommended by Forscheimer and Shattuck frequently modify nervous symptoms. Phosphate of soda, suggested by Trachewsky and indorsed by Kocher, or the glycerophosphate of soda, certainly control tachycardia and nervous unrest in not a few instances. Belladonna I prefer to digitalis or strophanthus; salicylates, sulphanilate of soda, intestinal antiseptics have availed little.

Despite reports of Goutschomkov and Mankovsky, endeavors to produce a specific thyreotoxic serum have as yet been abortive. Gley first suggested that deficiency of parathyroid function might be a chief factor in etiology of exophthalmic goiter. MacCallum found the parathyroids four times in eight operations for exophthalmic goiter; twice they were smaller than usual and twice degenerated; in one acutely fatal case none were found. Benjamins found them apparently normal in three cases. Moussu saw no result in one case from feeding parathyroids of cows. MacCallum reports feeding 12 glands daily for some weeks in a case of moderate severity without effect. From evidence yet at com-

mand it is not possible to say that the parathyroids in any way influence the affection.

It is not possible to dwell on results of operative treatment, though I am convinced that many cases belong to the surgeon. Five of my cases have gone to operation. In four improvement was almost immediate and the patients have remained well. One woman died four days after operation, with symptoms suggesting parathyroid insufficiency. It has seemed to me that more attention in operating should be given to the statement of Horsley, that division of the isthmus is sufficient to lead to retrogressive changes and shrinking in the rest of the gland. I have had no experience with the *x*-ray treatment as advocated by the Mayos and Beck.

In the last years effort has been made to develop a specific treatment of exophthalmic goiter. Ballet, Enriquez, and Lanz were pioneers in the movement. Lanz suggested that milk of dethyroidized goats might contain substances antagonistic to the exophthalmic goiter poisons. Burghart and Blumenthal from Leyden's clinic first used serum from a myxedema patient with encouraging result, and later introduced "rodagen," a precipitate from the milk of dethyroidized goats. Leyden, in *Die Medicinische Klinik,* reviews results attained and thinks them definitely favorable. Improvement is noted in three or four weeks, but treatment must be continued for months. Kollaritis reports three cases treated four to six weeks with rodagen without effect. Kuhnemann reports betterment in one case under 6 grams of rodagen daily. In 1901 Moebius communicated three cases somewhat improved by serum of dethyroidized goats. This has been put on the market by Merck and is given internally in 5-gram doses every second day, being administered in wine. Moebius has since reported benefit in 2 cases, Schultes in 1, Rosenfeld in 1, and Indermans, Boerma, Hempel, Lomer, Duerig, Peters, and Thienger in others. Thienger gives account of an acute case responding quickly to the

serum, of two with improvement, and of one with no result.

Such a new method of treatment must be most conservatively judged. I have had experience with rodagen in three marked cases over periods of four to eighteen months. In one severe case, 6 grams daily were given for four months with no appreciable effect, and the woman was later operated on successfully by Dr. T. W. Huntington. In a woman with marked nervous symptoms, insomnia and tachycardia, all symptoms seemed definitely to improve under five months' treatment with 6 grams daily; the moderate exophthalmos is unchanged, but the pulse rate is normal and the struma is smaller. A third woman has been taking 6 grams daily, off and on, for eighteen months. She had suffered from tachycardia, insomnia and nervous unrest for years. Sodium phosphate, bromids, salicylates, bromid of quinin and electricity did not control symptoms, and she refused operation. She had supraclavicular fat pads and the peculiar skin infiltrations described above. Rodagen has seemed to control the pulse for months as nothing else did, and she is enthusiastic over its effect on insomnia. After four or five weeks of steady use, she complains of depression and weakness, and has to stop for two weeks. Fat pads increase during rodagen administration, and two or three times the experiment has been tried of giving her iodid of iron in small dose. This each time promptly brings return of tachycardia and nervous symptoms, but modifies skin infiltration. Rodagen would seem to be of some benefit in these cases, therefore, but I would pass judgment only after a long series of cases. My experience with thyreodectin has been too limited to report. Dr. W. F. Cheney mentioned a case in which it seemed to control the heart symptoms. Dr. P. K. Brown tells me of a woman who grew worse rather than better under four or five weeks' treatment.

The whole question of the thyroid and its influence on development, metabolism and decay is a fascinating one.

It would be valuable to report more fully the early history of patients with myxedema and exophthalmic goiter, to classify more carefully early heart, digestive and skin symptoms of the latter affection. I have seen two paroxysmal tachycardia cases that developed later exophthalmic goiter. In one woman peculiar general pigmentation with vomiting, diarrhea and weakness had led to diagnosis of Addison; Oppenheim mentions a similar case. I have under observation a man with Parkinson who presents thickening of the skin of face and extremities as described by Fraenkel and Lundborg. A woman who has twice had eclampsia came to me with a large thyroid and symptoms suggesting beginning myxedema; she is interesting in view of the work of Nicholson, Lange and others on the relation of thyroid to eclampsia. The possible influence of the thyroid in California as an etiologic factor in our very common arteriosclerotic and renal affections should be remembered.

DISCUSSION.

Dr. James J. Walsh, New York, stated that he has tried the effect of paratyphoid extract, though without getting very encouraging results. About three years ago Dr. McCallum of Baltimore suggested a connection between the parathyroids and the symptoms of Graves' disease. Many years ago Professor Gley made investigations on this subject, and came to about the same conclusion. It seemed thoroughly justifiable then to try the effect of the drug. Dr. Walsh treated four patients. In two milder cases the parathyroid seemed to be of benefit. In two severer cases, it not only gave no relief, but seemed to make some of the symptoms worse. It is doubtful if the parathyroid extract was entirely pure and free from thyroid material, although every effort was made to secure it in the pure state. It must not be forgotten, he said, that younger patients, that is, those under 25, frequently get better, even with marked symptoms, under almost any treatment. It is surprising to note how severe some of the cases are and how complete the recovery. Intermissions are extremely common, and may well be attributed to treatment when they are only phases of the disease. In older patients intermissions are rarer, and it is on these that new remedies must be tested if there is to be any reliance on the results.

Dr. E. F. Wells, Chicago, said that it has been his fortune

to see many cases of exophthalmic goiter, and no patient who had been treated for any considerable time before coming under his observation, but had been given thyroid extract, and invariably with the effect of increasing the symptoms. He is sure that there is an impression in the profession that thyroid extract is the remedy for exophthalmic goiter, and a warning as to the danger attendant on such treatment is eminently desirable. Empirically, Dr. Wells has found that codein is extremely useful in these cases. He gives from one-quarter, one-half or three-quarter grain three or four times a day, and for months with perfect immunity. The patients bear it well. After an experience with this remedy for eight or ten years, he is led to advocate it as the most efficient for the purpose of any which he has any knowledge.

Dr. G. W. McCaskey, Fort Wayne, Ind., emphasizes the importance of noting the spontaneous fluctuations that occur in some of these cases of a very chronic character with any line of treatment and sometimes without any treatment. He has had two patients under observation for a period of ten or twelve years, which have exhibited these peculiarities to a striking degree. At times they appeared symptomatically well, and one of them has remained so for one period of two or three years, but in both cases the characteristic syndrome has infallibly returned. Due allowance must be made for these variations in estimating the value of treatment.

Dr. George S. Whiteside, Portland, said that the type of thyroid enlargement seen in Oregon is a very mild one and much more prevalent among women than men, and more among the young than the old. As a rule, these patients present no symptoms. The condition seems to increase at the time of pregnancy and goes down afterward. Goiter in dogs is not uncommon in Portland. Exophthalmos seems to be the exception in both men and beasts in Oregon, but Dr. Whiteside has heard that it is much more common in California.

Dr. C. R. Grandy, Norfolk, Va., thinks that there are many more cases of enlarged thyroids in the United States than were formerly thought, simply because physicians had not been looking for them. In his own practice he has seen a considerable number of cases. When occurring in young girls he does not do anything for them. There is one class of goiter with a decreased secretion, which, as a rule, occurs in fat women with slow pulses. In such cases thyroid extract would do good. In the other class of cases there is an increased secretion which occurs in nervous people, with fast pulse rates, etc. Here the thyroid extract does harm. Dr. Grandy has seen two rather remarkable cases occurring in women past the menopause, in both of whom hysterectomy had been performed for fibromyoma for several years previously. In one there appeared to be a malignant change in the thyroid. The other woman passed from observation. In both cases there was not enough

thyroid secretion; one patient seemed to improve with thyroid extract; the other had some of the symptoms of myxedema.

Dr. J. A. Lichty, Pittsburg, Pa., agreed with Dr. Moffitt that it is a difficult thing to make a diagnosis when there are so few symptoms; and yet he knows of no disease in which an early diagnosis is so essential as in exophthalmic goiter. A great deal of harm may be done in a very short time if the disease is not recognized. There may be several so-called cardinal symptoms, but only these are necessary to make a diagnosis, i. e., rapid pulse, tremor and exophthalmos. If any two of these are present it is perfectly safe to place such a patient on treatment for exophthalmic goiter. If the patients are young girls, who are fond of dancing, bicycling, gymnastic work, etc., they should be warned of the danger and the harm that might result because of an existing exophthalmic goiter. These exercises should at once be forbidden. Dr. Lichty has tried the α-ray treatment without any benefit in these cases. During the past ten years he has cured two patients with the rest treatment. He emphasized the importance of an early diagnosis in exophthalmic goiter.

Dr. Christian Jonsson, Clinton, Iowa, said that young people seem to have a tendency to spontaneous recoveries, and that this disease seems to be more dangerous in old people. He has observed that thyroid gland treatment is extremely harmful in most of those cases, and it is his conviction that it should never be used in exophthalmic goiter. The treatment should consist in rest and freedom from worry, besides a tonic and sedative drugs, such as we have in a so-called sumbul tablet, containing iron, arsenic, sumbul, asafetida. In a number of cases this has given Dr. Jonsson surprisingly good results.

Dr. Herbert C. Moffitt, San Francisco, declared that he did not agree with Dr. Walsh that cases of exophthalmic goiter in old people necessarily go wrong. He has seen not a few such patients kept comfortable by routine medical treatment, giving such clinical evidence of further thyroid changes and slipping slowly from symptoms of exophthalmic goiter to those of myxedema. He mentioned one case in which stomach and intestinal symptoms were so marked that the affection was considered primarily a stomach one. After instituting the proper treatment the patient, a woman nearly 60, went along well, and is now showing signs of myxedema. The pulse rate is normal and the skin changes are those of myxedema. Dr. Moffit is of the opinion, in the light of our present knowledge, that marked cases of exophthalmic goiter are helped but not cured by medical treatment, and that such patients should be referred to the surgeon.

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THE SECRET NOSTRUM EVIL.

FRANK BILLINGS, M.D.
CHICAGO.

I shall make no apology for bringing this subject before this Section. Its importance to the profession of medicine and to the public justifies an exposition of the evil now. In no other country has this menace to the welfare of the people and to the best interests of scientific medicine developed as it has with us.

Probably the reason is that other countries, with one or two exceptions, protect the people against frauds in foods, medicines, etc.

Some day it is to be hoped that the Congress of the United States will enact a national pure food law which shall include the regulation of the copyrighting and exploitation of proprietary and other medicines.

Just here it will be well to say that the term "proprietary medicine" does not necessarily stamp a preparation or remedy as a nostrum. Webster says that a nostrum is "a medicine, the ingredients of which are kept secret for the purpose of restricting the profits of sale to the inventor or proprietor; a quack medicine." Some proprietary medicines are patented, or better, the process of manufacturing an article is patented. This patent protects the discoverer, or owner, in the manufacture of the medicine or drug for a period of 17 years. These preparations are ethical, in that they are not secret, for any one for a small fee may obtain from the patent office of the government a copy of the description of the process of manufacture and the actual chemical

composition of any such patented drug or remedy. The chief harm which has come to us in America from the protection by patent of the process of making a chemical or drug has been the resulting high price of the product. Many of the synthetic chemical drugs, like antipyrin, phenacetin, etc., cost ten times their worth as compared with the price of the same drugs in Germany and in other countries. As stated, however, such really patented preparations are not secret; the composition is known. Some of them are of value therapeutically. Many of them are valueless. Some of them are harmful. Most of them we could easily get on without and fare better with the older, more simple remedies. Too many "made in Germany" specifics are shoved under our noses.

Now, as to the other proprietary medicines. All the so-called "patent medicines" put on the market for the public, and many of the preparations exploited to physicians and distributed by them to the public, are not patented, but are protected by a copyright or trade mark. Technically there is no difference between the secret proprietary medicines manufactured for physicians' use and the "patent medicines" exploited to the public. Both are protected by a copyright or trade mark name. Both are protected for an indefinite time. They are mixtures, as a rule, of several ingredients.

The relation of the physician to these preparations, however, is very different. Those "patent medicines" which are advertised to the public are not considered ethical and physicians abhor them and rightly condemn their use because they are often dangerous and always irrational as remedies. On the other hand, the manufacturers of those copyrighted proprietary medicines which are exploited to physicians by extravagant claims of specific therapeutic action, use the doctor as the middle man to distribute the cure-alls to the public.

Medicines so prepared that the busy physician could easily dispense them found a certain class of doctors

eager to use them. The indications for use appeared on the label or in the accompanying literature. Tonics, blood and tissue builders, emmenagogues, pain relievers, febrifuges, laxatives, calculi dissolvers, soporifics, bile promotors, heart tonics, cures for Bright's disease, etc., have appeared in countless number and some remedies offered are confidently presented as cures for not one, but a half dozen diseases or symptoms complex. Indeed, the claims of many of the promotors of this class of remedies do not differ in extravagance from the cure-all patent medicines offered directly to the public.

It has been easy to obtain testimonials of the alleged value of many of these remedies. Many even of the "faculty" have extolled them. Why, therefore, should not the less experienced physician use these "elegant," palatable, all-ready to use, with label-specifying-dose, disease-indicating remedies? Prominent physicians and the "faculty" had testimonials in the circulars sent with the samples indicating the virtues; why, therefore, use the simple proved remedies of the pharmacopeia, and especially as the latter would often necessitate the trouble of writing a real prescription.

To the rational physician most of the mixtures, even with the formulæ, are objectionable. Disease is never quite the same in different individuals, nor does the picture remain the same from day to day. The treatment must be modified to meet the varying problem of the morbid process. Rational therapy calls for simple prescriptions; but if there be an objection to mixtures with fixed and known formulæ, what must one say of mixtures of secret or semi-secret composition?

As Dr. Horatio C. Wood, Jr.[1] says:

A much more elusive and therefore dangerous evil lurks in the class of mixtures which attempt to cloak their secrecy with a deceptive show of frankness. I think you will grant that the physician is rarely justified in the use of remedies concerning which he has no knowledge, and I maintain that

1. "Proprietary Therapeutics," The Journal A. M. A., June 10, 1905, p. 1836.

the publication by a drug firm, of whose integrity the physician is absolutely ignorant, of a professed list of ingredients of some mixture is not sufficient knowledge to pardon or to warrant the uses of that remedy. In the first place, if the published formula be correct, it is not enough to know simply the composition of a mixture, the exact quantities must also be known; there is a vast difference between the effects of 1 grain and of 100 grains of opium. Moreover, there is no means of knowing that the formula is a true one, for many of these corporations do not hesitate to pervert the truth.

Many of the promotors of these preparations claim, as chemists or as pharmacists, to be the discoverers of the wonderful remedies and the alleged unusual knowledge of chemistry or of skill in pharmacy has enabled the discoverer to develop in a mixture heretofore unknown, therapeutic qualities. Truth to tell, however, it is known that the proprietors are not always the manufacturers of the preparations they exploit and distribute. Many of the proprietary preparations are made by the large manufacturing pharmacists for the owners. Pharmaceutic skill is doubtless used in these instances, but it is the kind of skill which is for sale and is not personal.

I am informed that it is not unusual for one manufacturer of proprietary mixtures to have several so-called "companies," through which he can more easily exploit and distribute his products.

There is said to be a direct relation between the Dad Chemical Co., the Od Chemical Co., the Sultan Drug Co., the Rio Chemical Co., and the Peacock Chemical Co., or at least that they are linked together through one individual, and that Battle & Co. and the Lambert Pharmacal Co. are related to the above list. It is said, too, that the Vass Chemical Co., the Lotos Chemical Co., and the Valley Chemical Co. are one combination. Doubtless other combinations exist.

Curiosity recently prompted me to look through a number of medical journals and I can not resist the temptation to quote some of the preparations advertised

in them: Aletris Cordial, Celerina, Neurilla, Respiton, San Metto, Cactina Pellets, Seng, Chionia, Thialion, Zarcol, Ecthol, Hagee's Cordial of Cod Liver Oil Compound, Mandragorine Tablets, Rheumagon, Ponca Compound, Ammophenin, Chloro-Bromon, Anasarcin, Bronchiline, Zematol, Zymoticine, Sulphogen, Labordine, Satyria, Manola, Cacodol, Eusoma, Leprosen, Sulpho-Naphtol, Pasavena, Neurosine, Germiletum, Bonn's Passiflora Tablets, Dioviburnia, Tongaline, Lithiated Hydrangea, Melachol, Gonoseptone, Calicolo, Solsul, Saliodin, and so on *ad infinitum*. These are only a few samples of what the physicians of the United States are asked to prescribe. But there are hundreds of secret preparations that are not advertised in medical journals, whose literature and samples come to us through the mails, etc. In the majority of cases, we do not know their contents, and in many instances an analysis shows that they are simply mixtures. Often a prescription written by a physician for a particular case is purloined, put up under a trade-name and exploited as a cure-all.

As an illustration see the official announcement of the Council on Pharmacy and Chemistry regarding certain nostrums that have been exploited as synthetic chemical preparations guaranteed to cure everything. I have no doubt that the majority of the physicians who have been prescribing phenalgin, antikamnia, sal-codeia (Bell), and ammonol were shocked when they found out that, according to the analyses, they had been giving a simple mixture of acetanilid, with bicarbonate or salicylate of sodium or carbonate of ammonium, with a little caffein in some instances. What physician will be foolish enough to use these preparations, when he can get the same of his druggist for at most one-tenth the cost, but especially what physician with a particle of medical knowledge would think of giving acetanilid if he knew it, in the majority of the conditions in which, according to the advertisers, these nostrums are indicated?

What physician would prescribe Gray's glycerin tonic, if he knew that its chief ingredients are gentian, dandelion, glycerin and sherry wine?[2] Could he not write a prescription as good and feel that he was his own judge of what constitutes a tonic?

Let me quote from THE JOURNAL A. M. A.[3] This, I am told, refers to an article advertised as a cod liver oil preparation—one of the tasteless kind, that has been investigated by a subcommittee of the Council:

> We have recently had occasion to open a package of a well-known "Tasteless Cod Liver Oil" preparation. The circular which was wrapped about the bottle was replete with interesting information, especially for the patient, who obtains the remedy in the original package, as prescribed by his physician. He finds in it a list of the diseases in which the preparation does wonders—they range from the dread consumption to cystitis and hemorrhage of the kidney. Most interesting to us, however, is the statement that this compound "contains all the necessary elements of nutrition." It is too bad to disturb this beautiful vision by the report of the chemist. This shows that the product is quite free from oil or proteids; the only nutrient ingredients are alcohol, sugar, and perhaps glycerin. But the claims of the manufacturers are probably correct, for it contains carbon, hydrogen, oxygen, and probably a trace of nitrogen—so does gunpowder.
>
> Perhaps it will now be the turn of strychnin to be advertised as the ideal food. It seems superfluous to point out the moral of this tale.

It is not necessary to enter into a discussion as to whether we should ever prescribe secret proprietary medicines, for in the minds of intelligent men, even with only a smattering of medical knowledge, there can be but one answer. A physician who has a true appreciation of his responsibilities, who has even ordinary knowledge of the action of drugs, and the danger from their unintelligent use, would not think of prescribing for the sick, who have placed themselves under his care, a preparation about which he knows nothing except what

2. "Each half ounce is stated to contain dilute phosphoric acid, 12 minims; gentian root, 10 grains; extract of taraxacum, 15 grains; glycerin, 80 minims; sherry wine, 80 minims; carminatives, q. s."—"Thesaurus of Proprietary Remedies," p. 148.

3. June 17, 1905, p. 1943.

the manufacturer, about whom he knows less, had told him. While there is no excuse for prescribing these medicines, too, many unthinking physicians are influenced to do so by the claptrap designated "literature," which the exploiters publish about their preparations.

There is not a secret proprietary preparation that has any more value, from a pharmaceutical or therapeutic standpoint, than has the ordinary prescription of the average general practitioner. Stop advertising them and they would be forgotten, just as "patent medicines" pass away if they are not advertised. A review of 10 or 15 years will call to mind many concoctions which physicians were asked to prescribe, and which, according to the advertisements, performed wonders, but now are heard of no more. Their advertising literature stopped coming and the nostrum-prescribing doctor ceased to use them.

What is the cause of the nostrum evil? There are several.

1. Pharmacology and therapeutics are neglected relatively by many of our medical schools. Anatomy, physiology, pathology, diagnosis, etc., are emphasized and too often the usefulness and limitations of drugs are neglected. Too frequently drug nihilism is taught. If the student were fully taught the physiologic action of drugs, the art of prescribing, preferably single remedies or in simple combination, using if he desires the pharmacopeial preparations prepared by reliable manufacturing pharmacists, and at the same time if he were taught when not to rely on drugs, but frankly to prescribe for his patient a course of hygienic measures which alone would accomplish all that would be required, he would not be the willing dupe of the nostrum vendor, as he now is.

2. The reputable manufacturing pharmacists deserve great credit for the improvement they have made in pharmaceutical products. They have afforded us of-

ficial preparations in the form of pills, tablets, syrups, tinctures, extracts, etc., which are elegant in appearance, often palatable and usually potent.

For this advance in pharmacy, a distinct credit to our country, we owe them our thanks.

Unfortunately, many of them have not stopped at this point, but have manufactured their own special mixtures which are just as objectionable as the products of the special manufacturers. They, too, have been active with their agents in visiting physicians and in distributing "literature." This encourages drug-giving in specific mixtures for special symptoms, and is wrong. With one hand they do good work, with the other much evil is done.

3. The nostrum makers at first copied the methods of the reliable manufacturing chemists, in exploiting their products, but they have gone a step further and have reached a point where one may say that they have subsidized the medical press. I know I am on dangerous ground when I make this statement, but right here is the chief cause—and the remedy. How many of our so-called medical journals are subsidized by medicine manufacturers I do not know, but all physicians know as well as I that there are many, and I do not refer to the so-called house organs. I unhesitatingly affirm that one-half of the medical journals of the country would be out of existence if it were not for the nostrum advertisements. Under the circumstances, therefore, can we expect these journals to say anything? Need we be surprised that scarcely a journal published the official report regarding the acetanilid mixtures, when the preparations hit were the best paying advertisements in the country?

What is the remedy? Publicity. The enlightenment of the profession. The truth regarding not only what the preparations contain, but who makes them. Certainly no honest manufacturer will object to this last

proposition, and no honest physician will put up with less than the former.

The Council on Pharmacy and Chemistry has been created to investigate the non-official preparations, to find out the truth about them, and to publish its findings. It is not necessary to repeat here the results of the work already done by this body. All physicians have read, or may read all about it. In my opinion there has been no movement undertaken by the American Medical Association that will be so far reaching as this one to rid us of the blight of the nostrum evil. For the first time, we see the possibility of the elimination of a part, at least, of this curse to American medicine. It is the first practical solution offered of a most difficult problem.

But—and I want to emphasize what I am about to say—the movement will have the most determined opposition that money can bring. Millions are being made annually by the nostrum manufacturers, and they will not sit idly by and see this wealth-producing business done away with if they can prevent it. It won't be an open fight, for their business will not stand publicity. They will have with them those so-called medical journals which are published solely in their interests.

This movement will have the sympathy of every thinking physician of the country, but sympathy does not win battles. In this fight those who are representing us should have all the support we can give. In society meetings especially we should aid in the propaganda by helping to enlighten and to interest those of our profession who have given the matter no thought. We should support those journals that represent us, and not tolerate in our offices those that we know to be subsidized and to represent their advertisers rather than their readers.

DISCUSSION.

Dr. John H. Musser, Philadelphia, said that the cordial reception of this paper indicated that the members of the Sec-

tion are in full accord with the sentiments expressed by Dr. Billings. He said that the nostrum evil as defined by Dr. Billings stultifies the profession in many ways. First it robs the physician of that practice of nice discernment in the choice of remedies, of their indications and their doses, which is essential to the full development of therapeutic skill. A physician's chief asset is experience, but what experience of the value of a remedy can be acquired when it is used in the manner in which we are instructed to administer it by the audacious five-dollar-a-day peripatetic therapeutist? Second, it prevents a cultivation of the scientific therapeutic habit, for, if premises are wrong, how can conclusions be correct? The uncertain combinations in unknown proportions, of unreliable remedies, concocted by unscrupulous grafters, can not possibly form a true figure in a proposition. Consequently, no true conclusions are drawn, and, hence, scientific habits are very soon cast to the winds. Third, it engenders irresolution as to the value of remedies. They are given in a half-hearted manner, and consequently a minimum effect is produced. A physician who prescribes with a clear knowledge of the effect of a remedy gets a surer and more immediate response. Doubt causes inaction. Fourth, it destroys scientific habits. If a scientific habit is not employed in our work, we are not truthful in our action. This lack of the worship of truth in treatment soon engenders a want of exactness in diagnosis. In consequence, a slovenly habit of practice in general will follow. Fifth, the doubt of the value of drugs and of medical measures is soon transmitted to the laity. Is it any wonder, Dr. Musser asked, that all *isms* flourish when physicians can not support their own therapeutic actions by experience or by scientific induction? The fact that every three years, perhaps less, the whole type of nostrums changes shows that experience has not been garnered. Time alone enables physicians to gather knowledge which the nimble "nostrum-mer" or drug drummer would prefer us not to have. Sixth, the nostrum evil threatens the enlightened principles of modern medicine. Our great glory is in adhering to the line of conduct of the tenets of Hippocrates and of Sydenham. "Do good or do not harm." It is not the use of drugs, but it is management and measures that mark our later-day progress. By the nostrum tenets, polypharmacy is essential and excessive drugging is the rule, both contrary to modern medical practice. Seventh, the nostrum evil stultifies physicians, because it makes them dishonest. They can not be honest if they prescribe things of which they know little or nothing. Dr. Musser urged medical men to be true to themselves and to hearken to the warnings of the paper. Concluding, he said: "Let us lash with thongs of indignation those tempters who, with literature that is beyond all measure untruthful, unscientific and presumptuous, and with words of rank sophistry are surely entwining us in a python-like grasp that will strangle us, to feed their coffers."

Dr. W. G. Moore, St. Louis, heartily agreed with the statement that there is no subject of greater importance than that embodied in the paper just read. He presented to the Missouri State Medical Association a paper along the same lines and feels greatly re-enforced by Dr. Billing's paper. If there is any infamy blacker than this that confronts the medical profession, Dr. Moore does not know of it. Nothing can be a greater curse than this subsidizing of medical journals. When Dr. Billings was mentioning the various companies, Dr. Moore thought he had been living in St. Louis, but, instead, he is at the other end of the canal and the stench reached him up the river. There are medical journals published to-day that should be placed in the sewer. The best efforts of medical men are demanded, and physicians should not only refuse to support, but should despise such journals as publish advertisements of these secret nostrums. He said that he could not understand how any one could trust a patient to the care of a man who would consent to give something that the hired man had taught him to use. The laborer is worthy of his hire, and Dr. Moore respects his mission, but he can not honor his employer. In a recent issue of a prominent journal Dr. Moore saw this statement regarding the treatment of gastroenteritis: "Apply warm all over the abdomen; place a cotton compress over it and bind on antiphlogistin (blue mud), and you will have no further need of doctors or medicines."

Dr. Alfred Stengel, Philadelphia, said that the nostrum evil is such an insidious one that the best informed may be taken in. As Dr. Billings has pointed out, these preparations are placed before physicians in such a way that, unless they have abundance of time to look into details, it is difficult to distinguish *bona fide* chemical preparations from untrustworthy mixtures. When the copy of The Journal containing the analysis of certain nostrums was issued, one of his colleagues asked Dr. Stengel if he knew that phenalgin was not a chemical combination. The physician in question was under the impression that it was and was greatly surprised to find that it was a mere mixture, subject to constant change and with no guarantee of its character. Dr. Stengel declared that it is important that the members of the Section on Practice of Medicine, as a body, should take a firm stand at this time. The remedy for many of the evils that affect the profession is in organized action. This association has a membership of 19,000; in addition to the members, from 14,000 to 15,000 other subscribers read The Journal; whatever attitude the members take officially and whatever point of view is supported in the editorial pages of The Journal will reach so large a number of readers that the association may confidently hope for a removal of such evils as it attempts to correct. Dr. Stengel said that he felt, therefore, that, as a Section, they should indorse the Board of Trustees in their appointment of a "committee" to investigate and to make public the character

of various substances or compounds offered as medicines and that they should indorse all that Dr. Billings has said.

DR. JAMES J. WALSH, New York, seconded the resolution presented by Dr. Stengel. He stated that, while he is in accord with others in blaming the medical journals, he wished to call particular attention to the fact that it is the members of the medical profession themselves who are most to blame. He said that there is no use in physicians hiding their shame behind objections made against the management of the medical journals of the country. The manufacturers of secret nostrums find only too many customers for their wares, and even in medical centers, where physicians are supposed to be well educated, the evil of prescribing secret nostrums of various kinds is very widespread. Within a few years, it has been shown that in New York City about 70 per cent. of all the prescriptions written contain some proprietary medicine that ordinarily would be expected to fall under the ban of professional use. Dr. Walsh has made it his business to secure information regarding these preparations whenever he could. On a number of occasions, when the agent of a firm has brought some new and especially seductive nostrum, hitherto unheard of, but recommended as good for nearly every ill that flesh is heir to, and a few others besides, he has inquired of druggist friends as to whether the new remedy was being prescribed or not. In nearly every case, he found that, within a month after the new remedy was so persuasively introduced by the agent, some physicians were prescribing it in their practice. This emphasizes the necessity for making the physician realize that in doing this he is selling his birthright for the proverbial mess of pottage and not always getting the pottage.

DR. W. O. BRIDGES, Omaha, Neb., said that he feared that the resolution does not reach far enough. An appeal should be made to the individual physician, whether he be a member of this organization or outside it. Dr. Bridges believes that a large number of physicians unconsciously and unwittingly prescribe these secret nostrums against which we are making war to-day. He stated his belief, if physicians discontinued receiving the journals which advertise these preparations, more than one-third of them would go bankrupt. A friend of his, an editor and publisher of a metropolitan daily, recently told him that, since the expose of the secret remedies by the *Ladies' Home Journal*, his paper had suffered a loss in advertising income of one thousand dollars a month. Dr. Bridges declared that the profession is largely responsible for the conditions which exist. Dr. Moore has stated that a large number of these journals should be thrown into the sewer, and Dr. Bridges believes that still better results would be accomplished if physicians declined receiving them at all, that they might be returned to the offices from which they emanate.

DR. J. T. PRIESTLEY, Des Moines, Iowa, said that the gradu-

ates of the various institutions in this country have had neither the time nor the opportunity to learn to dispense their medicines, and in this they certainly are weak. He mentioned the case of a bright young man who told him that he had ordered so much calomel to be placed in so much water and a teaspoonful given so often. It must be remembered that at times a very affable gentleman comes along and shows something that appeals to these young and untrained men. Dr. Priestley believes that the fault is in the teaching. If the young men were taught how to prescribe drugs as well as to give them, there will be much less of this nostrum evil.

Dr. John A. Witherspoon, Nashville, Tenn., said that too little attention is given to the actual bedside teaching of the management of disease. Most young men leave college with an imperfect knowledge of the physiologic action of drugs and imperfectly prepared to make any therapeutic application to a case in hand. Dr. Witherspoon blames the man who has the proper instruction and who takes the responsibility on his shoulders of caring for a human life without a due sense of that responsibility, and who prescribes drugs at the dictation of the traveling man. The medical man who continuously and constantly keeps on prescribing such secret remedies becomes narrow and contracted in his ability to handle disease and becomes like the negro in Mississippi who was given a new safety razor to use. Shortly after, the donor saw him and asked him how he liked his new razor, and the answer came that it was good for shaving purposes, but for marriages, social functions and funerals it was perfectly useless. Now that is the position of the physician who continuously prescribes these quack nostrums; he will become perfectly useless in the practice of medicine. Many men who publish journals are not men who can be considered as molding public or professional opinion in medicine. Medical men should continue to fight them, and also should make it appear disreputable for any journal to publish these nostrums.

Dr. Joseph M. King, Los Angeles, Cal., declared that some men with a good knowledge of the physiologic action of drugs, will yet grasp at every will-o'-the-wisp, but one of our troubles is that the rank and file of the profession have not an exact knowledge of materia medica and therapeutics. In several of the large clinics in this country which Dr. King has visited, a great deal is taught regarding diagnosis, but he heard very little concerning treatment, and it would seem that clinics are being held to teach diagnosis only, and not for the purpose of teaching therapeutics also. Of course, no man can successfully treat a case until he can diagnose it, but the patient pays for the application of what the physician knows regarding remedies. It is important that the physician should have a thorough knowledge of the weapons at hand, and then he will not be so prone to run after false gods.

Dr. A. B. Grosse, San Francisco, Cal., said that the physi-

cians of California are in full accord with the views expressed by Dr. Billings, or it might be said that Dr. Billings has practically expressed his sympathy with the work done by the California *State Journal* under the able leadership of Dr. Jones. Dr. Grosse disagreed with some of the views expressed that the nostrum evil flourishes through the baneful influence of the subsidized medical press and the lack of therapeutic tuition in medical colleges. Just as long as the nostrum can be found in the advertising pages of respectable and standard medical journals, the root of the evil will not have been reached. He said that this is no time to mince words and we may as well admit the error of our ways. Even the official organ of the association, THE JOURNAL of the American Medical Association, has had its advertising pages polluted by the nostrum manufacturers, and this in the face of an organized fight against the evil by the California *State Medical Journal.* Dr. Grosse urges immediately remedying these abuses. He said: "Let us purge the advertising pages of THE JOURNAL so that our hands at least may be clean."

DR. THOMAS MCCLEAVE, Berkeley, Cal., stated that all physicians in California are greatly interested in this matter. He referred to the fact that several speakers had mentioned journals published especially to cater to this class of preparations, and said that THE JOURNAL of the American Medical Association is as great an offender as any. This crusade, he said, was started by Dr. Jones, editor of the *California State Journal of Medicine,* who called attention again and again to the advertising in the columns of THE JOURNAL of the American Medical Association and was villified for so doing. Dr. McCleave said that he should like to add to the resolution offered by Dr. Stengel or to make an amendment to the effect that the Trustees be requested immediately to remove from the advertising pages of THE JOURNAL of the American Medical Association the advertisements of these nostrums. He said that, under the stimulus of criticism, much of this objectionable matter had been removed from the pages of THE JOURNAL, but that some still remains.

DR. CHARLES G. STOCKTON, Buffalo, said that Dr. Billings' paper will do good because of the fact that he has mentioned names, and it is in this that courage is shown. If the names were more frequently mentioned, carefully but strongly, the profession would soon be educated as to what is right and what is wrong. Many in the profession are not of a way to learn what they should regarding these agents. Dr. Stockton said that he believed that the committee of the Association will help if names are mentioned, if a list of objectionable preparations is published regularly in THE JOURNAL.

DR. ALFRED STENGEL, Philadelphia, added the following to the resolution he offered:

> "*Resolved,* That the Board of Trustees be requested to effect the removal from the pages of THE JOURNAL

of the American Medical Association of the advertisements of any nostrums."

He thinks that this resolution should be passed. Unfortunately, all the 200,000 doctors in the country have neither the time nor the facilities for looking into the composition of objectionable medicaments. It is desirable, therefore, that THE JOURNAL should contain no deceptive advertisements and that a list of desirable or undesirable remedies should be available to the profession.

DR. NORMAN BRIDGE, Pasadena, Cal., proposed an amendment that the Trustees be requested to remove the nostrum advertisements.

DR. R. H. CARTER, Victoria, Canada, said that, although he is not a member of this Association, he would like the Canadian Medical Association to be informed officially of what has been done. Physicians in Canada receive many secret nostrums and much advertising matter from time to time from all the different drug houses that Dr. Billings has mentioned.

ALBUMINURIA IN NEPHRITIS AND BRIGHT'S DISEASE.

ALFRED STENGEL, M.D.
PHILADELPHIA.

Nicholas Cotungo, in the latter part of the eighteenth century, called attention to the coagulable quality of the urine in cases of dropsy, and Richard Bright showed the relation of disease of the kidney to dropsy and albuminuria in the early part of the succeeding century. Subsequently the pathologic observations of Bright, of Rayer and of others seemed to establish the invariable association of these conditions. Pathologists of the new school of cellular pathology confirmed the relationship of albuminuria and dropsy with an inflammatory lesion of the kidney so that in the course of time "albuminuria" and "nephritis" became terms of nearly identical practical significance.

As time went on, however, some of the physiologic chemists found that transient albuminuria or cyclical albuminuria might occur without any evidence of lasting disease of the kidneys. In the ordinary course of practice, however, physicians have looked on albuminuria as significant of nephritis, unless the evidence in favor of some temporary congestive or other condition has been well nigh overwhelming. The determination of the proper relations of these conditions to one another was made more difficult by the classifications suggested by various pathologists and clinical pathologists who sought to distinguish a number of types of nephritis and laid down complicated criteria of differential

diagnosis, with the result that practically every form of albuminuria might be made to fall in some artificial group. The more accurate urinary examinations and the more careful medical diagnosis of recent years, however, have established the fact that it is necessary to distinguish between nephritis in the sense of the pathologist and nephritis or Bright's disease in the clinical sense.

It must be recognized that the kidney is a highly differentiated organ subjected to exceptional irritations in its important function of excretion, and that inflammatory lesions in the minute pathologic sense may be extremely frequent without of necessity leaving any lasting results. Furthermore, it is obvious that nephritis does not become a condition of grave significance until the pathologic changes have attained a degree of intensity or have involved a proportion of the kidney substance sufficient to interfere with the complex functions of the organ so as to imperil the general health. The presence of slight intertubular exudation, of moderate or even extensive, if uncomplicated, degeneration of the epithelia of the tubules, or of slight alterations in the glomeruli, would not justify a positive assertion that the case was one of Bright's disease in the clinical sense. The distinction, of course, is one of degree rather than of kind, but the point at which I am aiming is to bring out the fact that an excretory organ like the kidney is excessively prone to slight and transient alterations which in all probability will undergo satisfactory resolution without permanent impairment of the integrity of the organ.

Much difference of opinion has arisen on account of this discrepancy between slight pathologic lesions and functional or clinical manifestations. In all of the cases now in mind, albuminuria, the great criterion of nephritis, is likely to be encountered, and yet the pathologic conditions are frequently neither serious at the

time nor lasting and progressive in character. It is hopeless to attempt a classification based on minute differences in the pathologic findings, and for practical purposes the old clinico-pathologic classification is still the most satisfactory. According to this, two forms of Bright's disease may be recognized, the acute and chronic parenchymatous nephritis, and a third form of nephritis, somewhat different in its clinical course and effects, chronic interstitial nephritis. Individual instances of the first and second forms vary much in the actual pathologic lesions. Sometimes epithelial degeneration is paramount; at other times exudative changes are conspicuous; changes in the glomeruli are usually pronounced and hemorrhagic processes may be conspicuous. In chronic cases, fibrosis sometimes becomes nearly as extensive as in chronic interstitial nephritis. The pathologic picture, therefore, is variegated in the extreme. Contrasted with these cases and essentially distinct from them is chronic interstitial nephritis. Analogy would indicate that the acute interstitial nephritis of the pathologist, occurring in acute infections and toxemias, might go on to the development of the granular contracted kidney, but, so far as definite knowledge is concerned, it must be recognized that this is probably rarely the sequence of events and that practically chronic interstitial nephritis is usually one of the concomitants and generally a comparatively late one of arteriosclerosis.

At the present time chronic interstitial nephritis is recognized as constituting but a subsidiary part of a more general disease in the majority of cases; while, in older days, it was regarded as an independent condition. According to this later view, polyuria and albuminuria may be regarded as significant merely of a renal form, or a renal phase, of a general vascular disease.

Contrasted with these three types of permanent renal disease, there is a large number of conditions in which

the kidney is temporarily involved, in which evidences of renal irritation or inflammation exist, and in which the pathologist might discover some pathologic changes, though the subsequent course is one of rapid resolution. The mere element of speedy restoration is evidently not dependent so much on the extent as on the character and intensity of the renal trouble. Such cases are frequent in association with infectious febrile processes and with circulatory disturbances. It is in these cases that some of the clinical signs, especially albuminuria, of Bright's disease occur, and it is these that cause the difficulty in distinguishing between true Bright's disease in the sense of the clinician and the nephritis of the pathologist. Doubtless until some means have been devised for estimating accurately the functional capacity of the kidney, it will remain difficult for the clinician to establish positive diagnoses and prognoses in certain borderline cases, but in the meantime a close study of the general features of the cases in which albuminuria and casts are encountered, but in which lasting nephritis does not follow, will enable the clinician to avoid error in the majority of instances.

Before proceeding to further discussion let me emphasize with all earnestness that diagnosis in renal disease can not proceed from the urinary examination alone any more than can the diagnosis of cardiac disease from physical exploration alone, or that of typhoid fever solely from the examination of the serum for the reaction of agglutination. Taken in conjunction with the general symptomatology, accurate examinations of the urine are indispensable, but without the general conditions as a check urinary examination may be as misleading as would be the symptoms without the urinary findings.

It has interested me to look over the records of my private cases to determine how frequently albuminuria occurs in the run of cases in general office practice.

These figures have the advantage that they represent the results of a single examiner's work and from one method of examination (heat and nitric acid). In the great majority of cases several examinations were made at different times, an added advantage considering the frequency with which albuminuria occurs as a temporary condition.

Among 581 cases there were 51 cases of undoubted clinical nephritis or Bright's disease, exclusive of chronic interstitial nephritis. In all of these there was constant and more or less uniform albuminuria.

In 74 cases of arteriosclerosis there was more or less inconstant albuminuria, without casts in 16 and with casts in 58. A number of these cases might properly have been classed as chronic interstitial nephritis. In all of these there was constant and more or less uniform albuminuria. In practically all it may be assumed that a certain degree of chronic interstitial nephritis existed, though other manifestations of arteriosclerosis dominated the clinical picture.

In 187 cases there was occasional or less often constant albuminuria in association with acute infectious diseases, gout, diabetes, tuberculosis, syphilis, cystitis, pyelitis, cardiac diseases, movable kidney, gallstones and jaundice, stone in the kidney, in occasional cases of other diseases, in pregnancy, and in adolescents without discoverable disease.

In 41 cases, in gouty or so-called lithemic subjects, there was occasional albuminuria at times when the urine was excessively acid.

In 215 cases (37 per cent.) there was no albumin at any time. In 11 cases casts were found without albumin.

I am ready to admit the unreliability of statistics, but would vouch for the essential accuracy of these figures. It might seem at first that urinary examinations are of little value, if out of 581 cases albuminuria without Bright's disease occurred in 202, no albumin-

uria in but 215, and as an indication of Bright's disease in only 51. Closer examination of the records, however, establishes several important points.

With very few exceptions, the albuminuria of the supposedly non-nephritic cases was qualified as "albuminuria in traces," and with nearly equal frequency repeated examinations showed that the condition was fluctuating in degree or temporary in duration. The exceptions to these rules were for the most part cases of arteriosclerosis, in which, as I have said, there was doubtless always a greater or less degree of chronic interstitial nephritis, though the renal manifestations were not generally predominant.

To establish the frequency of albuminuria in cases of severe acute infections and in cardiovascular diseases I have collected the data obtained from my records at the University Hospital. Summarizing the records of a great variety of infections, it is found that among 176 cases albumin was present in 59 and absent in 117. Among 304 cases of typhoid fever albuminuria was present in 83, clinical nephritis in 14, and albuminuria was absent in 207.[1]

Among 154 cases of cardiovascular disease, albumin or casts, or both, occurred in 81, and neither albumin nor casts in 73.

Table 1 shows the conditions in different types of such diseases:

No.	Disease.	Albumin and casts.	No. Albumin.
1.	Aneurism	6	15
2.	Arteriosclerosis	10	6
3.	Myocardial disease	10	8
4.	Malignant endocarditis	3	1
5.	Aortic valve disease	8	7
6.	Mitral disease	29	26
7.	Combined valve disease	15	10
	Totals	81	73

1. In explanation of the lower proportion of non-nephritic hospital cases showing albuminuria as compared with my private cases, I must explain that the examinations in the latter were made with much more care to detect even the slightest traces of albumin. In addition to the greater experience of the examiner, an important factor in this greater accuracy was the use of a reflector of prisms which gives a light specially favorable to the detection of faint turbidity in the liquid tested. The method used was to heat only the upper part of the column of urine in the test tube.

In considering these figures it must be remembered that a certain number of the cases were instances of combined cardiac disease and Bright's disease, but it is equally clear that the large proportion of cases of albuminuria require a further explanation.

A careful scrutiny of the clinical course of these cases of cardiovascular disease showed that almost without exception the condition of the urine was extremely variable, and fluctuated in correspondence with variations in the underlying condition, so that the degree of albuminuria was in a measure commensurate with the degree of cardiac insufficiency.

I wish to refer very briefly to the occurrence of albuminuria in cases of secondary syphilis, because I have found in a number of cases that the discovery of albumin has been looked on with great apprehension. My experience in this field has naturally been limited, and I content myself, therefore, with calling attention to the fact that slight or sometimes considerable albuminuria is not infrequent in the secondary stage of this disease. It has seemed to me that active mercurial treatment might in some instances be the responsible agent, but I am sure that slight albuminuria occurs independently of this, and in my experience it has proved a matter of no serious moment.

Another subject on which I wish to say a few words is that of the special form of albuminuria found in amyloid disease of the kidneys. It is well known that in chronic forms of albuminuria, the serum albumin is in great excess of the globulin. The conditions are reversed in amyloid disease to such an extent that preponderance of globulin in a chronic case warrants a strong suspicion of amyloid disease of the kidney. In several cases I have in this way been able to recognize this condition even before sufficient amyloid disease of the liver or spleen had occurred to enlarge these organs and to make them palpable.

In conclusion, let me say that the purpose of this

paper has been primarily to direct attention to the fact that albuminuria is an extremely common occurrence in various general diseases and that, though it may in a sense indicate an inflammatory condition of the kidney, such inflammation or nephritis may be of merely pathologic rather than of clinical significance, unless the albumin is considerable in amount and more or less constant in occurrence. The nature of the accompanying tube casts must not be relied on too greatly to determine the seriousness of the renal lesion, and in particular the presence of an occasional hyaline cast or even the frequent occurrence of such must not be regarded with too much apprehension. The modern method of centrifugation and the consequent examination of quite fresh urine increases the likelihood of our finding casts, and there is often difficulty in distinguishing between the insignificant cylindroid of the mildest grades of renal irritation and the definite hyaline cast of more decided disease. Even the latter, however, is so frequent in cases of arteriosclerosis, cardiac disease, hepatic disease, jaundice and gouty affections without serious renal disease that its significance is more or less trivial, unless general clinical conditions accentuate the importance of its presence. I do not wish to convey the wrong impression that I estimate lightly the importance of urinary examination; far from it. But I know from much experience that a trace of albumin is too often magnified in importance in the physician's mind, and that the clinical conditions as a whole are not sufficiently considered. Above all things, it is important in cases of suspected renal disease that the urine be repeatedly examined and its constant or fluctuating condition be taken into account.

CYLINDRURIA.

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The subjects of casts in the urine has been a favorite one for study in the clinical laboratory of the Johns Hopkins University during the past five years. In addition to such studies, this paper contains as its most important portion the report of a study of the records of all the cases of nephritis admitted to the medical wards of the Johns Hopkins Hospital, over 1,000 in number, about 500 of which came to autopsy, together with other cases clinically resembling nephritis but with no anatomic evidence I and my associates in the laboratory wish to express our indebtedness to Dr. Osler for the use of this abundant and most valuable material.

CASTS; THEIR CLASSIFICATION AND FORMATION.

Casts have been classified as cellular, granular and amorphous. The latter show no structure, being homogeneous or at the most with only a faint striation. All combinations of and transitions between these forms occur.

(1) *Epithelial Casts.*—These are made up of, or have attached to them, renal epithelial cells; that is, cells which vary much in size but have always (when it is visible) a round nucleus. The cells are flat and polygonal as a rule, not spherical. The protoplasm is usually (always ?) very much degenerated, the cell being but a mass of fat, myelin, or albuminous granules,

which may swell the cell to a great size. When these cells retain their finer structure, which is not often, they are considered to resemble those from the straight collecting tubules, not the secretory cells. An epithelial tubule could not pass a loop of Henle of normal bore, but single cells or the detritus of cells from above could attach themselves to a cast forming below. Most epithelial casts are masses of epithelial cells united by a hyaline matrix, but some are certainly desquamated portions of the tubules with the lumen, and with even the intercellular protoplasmic bridges visible. In one kidney which we have had an opportunity to study, in sections at the juncture of cortex and medulla the invaginated tube of epithelium could be beautifully seen, which, breaking loose, would be a cast. That is, at these portions were two tubes of epithelial cells, the intact one lining the tubule and an invaginated also intact interior one, evidently loosened and rolled down from above. Such perfect fragments are called "epithelial tubules." This being the origin, it is the free surface of the cell which forces outward the base lining the lumen.

All transitions between these and the coarsely granular and fatty casts are seen, and the question arises where to draw the line. In this laboratory we consider the cast epithelial if the cell outline of one cell with a round nucleus can be made out.

Also a hyaline cast with one epithelial cell attacked ranks as an epithelial cast.

We doubt, with Cabot, that all the mononuclear cells are renal; also that from study of the degenerative changes or "atrophy" of these cells any conclusions concerning the changes in the cortex can be drawn, yet we believe that the cuboid or flat polygonal cells are of renal origin.

(2) *Coarsely Granular Casts.*—All transitions between epithelial, leucocyte and these casts can be found. These are of a yellowish-brown color, very opaque, hence conspicuous objects, covered by coarse granules. Some

of the granules are soluble in acetic acid, hence of albuminous nature; others are soluble in ether and take the fat stains; still others resemble the myelin of the sputum. These casts are probably either epithelial casts the cells of which have undergone degenerations, or are agglutinations of the detritus of epithelial cells which have gone to pieces in the tubule before or after desquamation.

In the laboratory we have had occasion to study another form. In cases of subacute nephritis large cells sometimes occur, two or three times the size of an ordinary renal cell, or even larger, which are masses of fat and myelin droplets and resemble colostrum corpuscles. We believe these to be of renal origin. In some cases these cells occur in rows of two or three; in others the cell divisions are indistinct, while still others form typical granular casts. Among the coarsely granular casts are included hemoglobin casts, which are of a brownish-red color.

(3) *Fatty Casts.*—These striking objects are masses of fatty granules often preserving the outline of the original epithelial cells. They are yellowish or even blackish in appearance and soluble in ether; fatty acid crystals may project from them. The fat globules may be enormous, almost as large as a cell. They occur especially in malarial nephritis.

(4) *Finely Granular Casts.*—The term "finely granular" is indefinite. It includes casts very similar to the coarsely granular save that the granules are much finer; also many with little resemblance to these latter, since they are almost translucent, much smaller, less conspicuous, and are covered by, or have scattered over a part, very fine granules which are seen to belong to the cast and not to be a mere deposit on a hyaline cast; many of them are intermediate in appearance.

(5) *Waxy Casts* (also called colloid or amyloid).—These casts are very refractile, sharply contoured, often of a white or yellow color, homogeneous, and show a

great tendency to split transversely, hence they are fissured and are often in small fragments. They may have, rarely, cellular elements attached. They show a marked tendency to spiral twisting. Two groups are present, the clear white and the yellow; the first look as if cut from paraffin, the second as if from wax. They seem to be formed of a stiff, firm, brittle material. They look broader than the hyaline casts. Some give the amyloid reaction as a whole, some in portions; more do not, and the reaction is seldom really satisfactory. Some observers deny having ever found a good amyloid cast (Cornil). They are quite resistant to acetic acid.

The name "waxy" is best since it signifies only physical properties, not chemical, as the term amyloid does.

Between this group and the hyaline casts is a very large group of casts which are perhaps the commonest of all, which have not quite the physical properties of the waxy, yet are more distinct and solid-looking than the hyaline, which name they bear. It is important to recognize that some of these have deposited on them fine granules from the urine, giving them the appearance of the finely granular cast.

(6) *Hyaline Casts.*—There are the coloid or glassy casts. They are pale, very slightly refractile, watery in appearance and difficult to see unless the light is almost shut off or unless one notices crystals or cells sticking to them. For this reason, and because they are so often few in numbers it is better to stain them with Lugol's solution, which gives a yellow color, or with gentian violet. If low light and no condenser be used, however, this is unnecessary. They give the microchemical tests of albumin. They may have the same cells attached as the other casts. They are beautifully cylindrical, with rounded ends, a uniform diameter as a rule but not always, may be either broad or very narrow, and sometimes are twisted like a corkscrew.

Hyaline casts sometimes have a fibrillar appearance

and may disintegrate, in which case they resemble a Curschmann spiral in miniature; that is, these consist of spirally wound threads.

Branching casts have been described. Some taper considerably along their length. Their outline is very regular. These casts occur in all conditions, but this is the only form which follows certain disturbances in which there is no question of inflammation. They are so different in appearance from the hyaline casts just mentioned as "intermediate" that they really deserve a separate name. They are easily dissolved by acid, or alkalies, are soft, elastic, and easily destroyed by cold or heat. They are the most important to recognize since they occur so often alone. They are the first to disappear in a urine which is becoming alkaline, hence the freshly voided urine should be centrifugalized and studied on a broad slide without cover-glass, which is covered well with the urine, and using the low power. Several slides should thus be examined before the search is abandoned.

Hyaline casts seem to be the ground substance for most epithelial, pus and blood casts, and hence for most of the mixed variety; one end of such a cast may be purely hyaline.

(7) *Blood Casts.*—Blood casts are a coagulum of red blood cells which have formed within the tubules. The term is also applied to any of the above casts with red blood cells attached. Some of the blood cells are so pale that it is hard to recognize them. Many have crystals of hematoidin attached.

(8) *Hemoglobin.*—Casts of hemoglobin occur in hemoglobinuria, the hemoglobin occurring in amorphous masses. Some seem to be other casts impregnated with hemoglobin.

(9) *Fibrin Casts.*—These are rare, if even they ever occur. They are opaque, granular, longitudinally striated, often ribbon-like and twisted, often fibrillar

and branched at their ends; in them are mixed fragments of blood cells and granules of pigment.

(10) *Pus Casts.*—These have a formation similar to that of the blood casts. The nuclei must be first seen and their polymorphous nature decided, to be sure it is not an epithelial cast. This may be done by adding acetic acid. Pus cells are smaller, more spherical and finely granular than the epithelial casts.

(11) *Cylindroids.*—We should prefer to separate these into two groups. The first are the so-called "mucous threads." Some are short, some are very long extending through several fields, singly or in snarls. They are flat ribbons of mucus which no one would confuse with a hyaline cast. Their diameter varies much, but on the whole they are narrower than hyaline casts. They are not cylindrical, but ribbon-like, as is well seen in their twists. Such threads make up the nubecula. They usually are branched and taper off into threads the ends of which it is almost impossible to see. They have a finely striated surface, sometimes finely granular. They do not dissolve on adding acetic acid.

(12) *Other Elements.*—In addition to these, and differing much from them in appearance, are seen elements which appear exactly like hyaline casts for the most of their length, but which at one end run off in a longer or shorter thread. They are often broader than hyaline casts, and are frequently not strictly cylindrical, but somewhat club-shaped. Those observers who are particular on this point exclude from the list of casts anything which has one end at all tapering or thread-like. These casts appear to be circular on cross section. They have not always the same fibrillar nature and are more refractile than mucus threads, hence are easily picked out in a snarl of the latter. They occur also in those circumstances in which casts would be expected and have the same significance. They occur when only a few hyaline casts are present, but a trace of albumin, and when the acetic acid precipitating body is abund-

ant; we have often been tempted to associate them in some way with this body. We are certain that for the greater part of their length they are like typical hyaline casts, and could the fine end be broken off, as we suspect is done by the centrifuge, the fragment without the tail could not be distinguished from a cast. Like the mucous threads and hyaline casts these threads may be covered by urates and hence have the appearance of granular casts. These, like hyaline casts, and differing from mucous threads, often have cells or detritus of cells attached. Chemically these bodies are like casts and are soluble in acetic acid. The point is of considerable importance, for mucous threads certainly arise from the mucous surface, while if casts they should arise in the renal parenchyma. They were first described as of the same significance as casts. It is perhaps safest to observe the old rule and exclude from the list all which have a definite tail on one end, and if, as often happens, one is in doubt to call it a cylindroid.

(13) *Combined Casts.*—These comprise nearly all the casts in most cases, and they are the hardest to classify. It is customary to call a cast with a recognizable epithelial, pus, or blood cell attached to a cellular cast, an epithelial, pus or blood cast, although many workers prefer to use the term "hyaline with leucocyte attached," etc. The most common mixed casts are hyaline and finely granular, or waxy and coarsely granular.

(14) *Bacterial Casts.*—Masses of bacteria in the shape of casts occur in purulent infectious pyelonephritis and in pyemic kidneys, but a cast also may become permeated by bacteria, either in the body or after being voided in the urine, in a remarkably short time.

(15) *Urate Casts.*—In uric acid infarcts of the kidneys of the newborn, masses of sodium urate may be found in the urine.

(16) *"Pseudo Casts."*—This term is used by some observers (Neubauer and Vogel), to mean a cast which is not a mould of the tubule, formed of some homogen-

eous material, hence the term included epithelial, pus and blood casts; but the term, we believe, should apply to origin, and the question is: Does it come from a tubule? It is not at all unusual for an urate sediment to assume the shape of a cast. All casts in a concentrated urine may become encrusted with urates and hence be of a dark, homogeneous granular nature. True granular casts are not homogeneous; they are coarser and more refractile than these pseudo casts which also have uneven edges and disappear on warming. Other salts forming such casts are uric acid, calcium oxalate phosphates, sodium urate and ammonium urate. Scratches on the glass are sometimes confusing.

Characteristics of Casts.—The length and the breadth of casts vary. Usually they are from .005 to .05 mm. in width. Their size may be from very small fragments to 1 mm. in length or longer. These very long casts are almost always hyaline. Some casts are almost on the limit of vision, but vegetable fibers must be excluded. Their diameter is that of the tubule. From the size of the casts no conclusions can be drawn of their source, so much does the size of the tubules vary in various conditions. It was formerly supposed that the beautiful corkscrew forms so often seen came from the convoluted tubules, but this is improbable, since any corkscrew shape would certainly be effaced during the passage through a straight tubule. Some are spiral all their length; others only at one end. This, says Senator, merely shows them to be composed of a tough, elastic material which has been squeezed through a narrow canal, or through a narrow orifice. The end of the cast is seldom split or forked.

Origin of Casts.—The origin of epithelial casts, especially of those with a lumen, is not disputed; yet they mean not necessarily a serious lesion, but merely desquamation of epithelium such as occurs from all mucosæ as the result of "catarrhal" inflammation; neither is the origin of blood and pus casts disputed. We believe

these casts, the epithelial, blood and pus, to be much more common than the usual urine records would indicate, perhaps since the general belief that they indicate a rather serious condition leads one to misinterpret or to pass them by when found in some trivial condition. As a matter of fact they occur whenever there is an acute, that is a sudden, disturbance of the cells, whether inflammatory or not. The coarsely granular casts quite certainly are formed from epithelial by a granular degeneration of the cells to the waxy casts, and all transitions from the coarsely granular may be found. This transition may also occur in the leucocyte casts, but is less true of the blood casts. Such transitions are supported best by the study of sections of the kidney.

The rapidity with which waxy casts may appear, unaccompanied by epithelial and coarsely granular casts, and the transitions between them and the hyaline, lead one to suspect that they differ from the refractile hyaline in only physical properties. One explanation is that they are hyaline casts which have remained in the tubules a long time and the originally hyaline or granular substance has become waxy through "amyloid metamorphosis." The sudden appearance of waxy casts may mean merely the washing out of those long in the tubules. We do not believe that the transition from epithelial cast to coarsely granular and from these to finely granular, and then to waxy, applies in most cases, but may for some. These transitions can not be followed in the casts when these are in the urine. Against this theory may be mentioned the sudden appearance of enormous numbers of one group without a corresponding increase of the so-considered previous stages. Waxy casts may appear in great numbers in the few last hours of life; the finely granular transparent casts in their occurrence bear almost no relation to the coarsely granular, as is best seen in the Kulz sign of oncoming diabetic coma. Yet the general ideas of their origin may still be true, and some casts may depend

on the disintegration of the epithelial cells, by which they are formed; this disintegration, together with abnormal secretion, occurs in the cell while it is still a part of the tubule and exposed to the toxins, etc., in the blood. That changes in the cell thus situated are sometimes rapid we are sure, but the free cell will not go to pieces nearly so rapidly as is imagined. At least the changes, whatever they are, occur in the tubules, not later. It is true that the casts show transitional forms, and that in one case two forms may be combined, but this could have been determined during the process of formation, as well as later. The importance of this intratubular determination of form is best seen in the waxy casts. These occur when the casts remain a long time in the tubules. Those in closed tubules are waxy; the casts following an oliguria are often waxy, which is seen best in cases of decapsulation of the kidneys for subacute nephritis. We can not give any better explanation for their appearance antemortem.

The origin of the hyaline casts, however, has long been in dispute, some observers claiming that they are an exudate into the tubules, others that they are a product of the secretion of the cells. These casts are certainly not coagulated fibrin, since they arise where there is no suspicion of inflammation, that is, in a practically normal kidney, as with the albuminuria of the newborn. The typical hyalines do not give the Weigert's fibrin stain. Two sources are possible: (1) That they are formed from the coagulated albumin of the blood serum, which escapes from the glomeruli, or perhaps, when diseased, through the tubules, and coagulated possibly by a ferment from the renal cells. Cylindruria, therefore, is visible albuminuria. According to this view, the difference between hyaline and waxy casts would be the amount and rapidity of excretion of this coagulable albumin, and the time it remains in the tubules. It is

an interesting idea that such albumin should coagulate, for where a certainly coagulable albumin is present, as in the case of chyluria, these casts are absent; also there is little relation between albumin and casts in amount, and either may be present without the other, yet albuminuria and cylindruria run too parallel to be independent. The one may always at least be suspected when the other is found, and in nephritis especially in their amounts they have a very definite parallelism. According to this view the materials for the casts escape some distance from the point where this material is collected and formed into a cast. (The ascending branch of the loop, the straight and the collecting tubules.) (2) Other observers (Key, Beyer, Senator, Langhans) claim that these casts originate in the epithelial cells. From sections of kidneys all steps of the process may be traced. In some cases epithelial cells die and undergo hyaline degeneration, and this substance may be molded to the cast; or the epithelium may die and allow lymph to transude into the tubule which, mixing with the cell detritus, coagulates; or (Oertel, Bartels, Rodiva, Aufrecht, Cornil, Brault) the very slightly injured epithelial cell still functioning may secrete a coagulable substance. This latter is the generally accepted idea. Some cells are seen to be swollen by globules; others have excavated edges, that is the vacuoles full of albuminous matter are discharged into the tubules and there fuse.

The origin of hemoglobin casts is interesting, since hemoglobin is soluble in the urine. It may be, however, that they represent hyaline or waxy casts impregnated with hemoglobin.

Chemistry of the Cast.—The chemistry of the cast is little studied. Probably none are fibrin. Some give an amyloid reaction when there is no such degeneration of the kidneys; amyloid disease rarely has such casts. Many react reddish to gentian violet; and brownish to Lugol's fluid.

A STUDY OF THE CASTS IN A SERIES OF CASES OF NEPHRITIS AND OTHER CONDITIONS.

We are obliged to consider other things than casts alone, albumin, etc., in this study that the picture of the cylindruria may be clearer.

Active Congestion of the Kidneys.—In one case of acute lobar pneumonia without, as yet, nephritis and with the kidneys actively congested, the weight was 425 grams, the depth of the cortex 7 mm. The urine was normal in amount, of a high specific gravity, with considerable albumin and a very few finely granular casts.

Chronic Passive Congestion.—In the urine, at first scanty, dark in color, and acid, albumin appears sooner or later in traces, although sometimes in good amount. Casts are present, chiefly hyaline, rarely granular, more rarely other varieties. A very few leucocytes may be found and still fewer red cells. The points of importance in this urine are the small amount of albumin, the large urate sediment, the comparative absence of renal epithelium, and the scarcity of granular casts and leucocytes.

Of 11 cases of extreme chronic passive congestion, chiefly heart cases, yet anatomically with no miscroscopic sign of nephritis, in 8 the clinical diagnosis of nephritis had been made. The average weight of the kidneys was 390 grams. The cortex averaged 8 mm. in thickness (7 to 10 mm.). The amount of the urine varied with the cardiac condition, being either normal or diminished in amount. The specific gravity was high, running from 1025 to 1027 in some cases, and in but 3 cases below 1015 for much of the time. Albumin was present in all cases; in one-half of them there was only a trace, but in others large amounts, even 0.6 per cent.

Casts were abundant in 3 cases and absent in but 1; as a rule they were few in number. Here in 3 cases, as in other conditions, on some days, they were present in extraordinary numbers; on other days there were

few, and these chiefly of the hyaline and granular varieties, but in some cases epithelial, pus, waxy and fatty were found.

Cloudy Swelling.—Twenty-three cases were chosen which at autopsy showed extreme parenchymatous degeneration without other evidence of nephritis. Nine of these cases were of typhoid fever, 4 of pneumonia, and the rest scattered, but all fevers. In 1 case of typhoid fever the clinical diagnosis of uremia had been made.

The average weight of the kidneys was 410 gm. (250 to 590 gm.) The cortex averaged 7.5 mm. thick (5 to 12 mm.). The urine of these cases voided from one to two days before death varied in amount from 500 to 1,900 c.c. and was of a rather high specific gravity (1015 to 1028). This varied inversely as the amount. In one case the specific gravity was for several days 1004, the amount averaging 1890 c.c. In the specimens just before death, albumin was present in traces in 12 cases, much in 5, and none in 2. The albuminuria had continued in some cases for two or three weeks; in one case the first record of its presence was 34 days before death; in the other cases it appeared much later. In 2 cases examined one week before death no albumin and no casts were present.

Almost all varieties of casts were present, particularly hyaline and granular, but also blood, epithelial, and waxy. Few were present as a rule; in 3 cases large numbers. Two cases were without albumin and without casts even to the very time of death. One was a case of tertiary lues of the brain, the kidneys showing exquisite parenchymatous degeneration and the urine a specific gravity of 1008, yet even on the day of death there were no casts and no albumin. In typhoid fever cases with the bacilli present in the urine in large numbers, repeated examinations showed no casts, although a fair amount of albumin was present. As a rule, the casts appeared later than the albumin. In one they

were very numerous on the last day of life. In 4 cases red blood corpuscles and epithelial cells were present.

Fatty Kidneys.—In the severe cases of fatty degeneration or infiltration of the kidneys the amount of urine is diminished, dark and cloudy, although it may be normal in amount. The urine is present in from traces to considerable amounts. The casts are chiefly hyaline and granular, some are fatty; there are a few red blood cells and a few leucocytes, although in some cases, many. There seems to be no relation between the number of casts and the amount of albumin.

We chose from our autopsies 7 cases with extreme amount of fat in the cortex and, microscopically, no other chronic change. The average weight of these was 380 grams (250 to 530); the cortex was from 6 to 8 mm. thick. The amount of urine was normal, and the specific gravity varied from 1020 to 1024. The albumin was considerable in about one-half of the cases, and there was only a trace in the others. In no case was albumin found two weeks before death.

The casts were hyaline and granular, few or many, the number bearing no relation to the amount of albumin. In 2 cases a few red blood cells were found, and usually some pus or epithelial cells.

ACUTE NEPHRITIS.

Acute nephritis has been divided into several various groups, chiefly from the standpoint of pathology, but for the clinician a division is very difficult. Senator separates the tubular nephritis or acute parenchymatous from the acute diffuse. In the acute parenchymatous form the tubules especially are involved and the glomeruli little or not at all. The clinical symptoms are slight or none. The urine shows only slight febrile albuminuria, diminished amount of urine of rather high specific gravity, and few or no casts. The mildest grade is simple cloudy swelling and from this are all gradations to the acute diffuse nephritis. The urine

contains often a heavy sediment, in some cases chiefly of renal epithelium, and hence the name "nephritis desquamativa." The epithelial cells may be single or in casts. Hyaline casts, few or many, are present. Crystals of uric acid and calcium oxalate, red blood corpuscles are often present, and hemoglobin in granular casts or masses. The leucocytes are usually few in number. The albumin is nearly always slight in amount, in remarkable contrast to the amount of sediment, and some claim that of this nearly all is nucleo-albumin from the cells.

In the acute diffuse nephritis, a good illustration of which is that following scarlet fever, the urine is diminished in amount; there may, indeed, be anuria for the first 24 hours. From 50 to 100 c.c. for the first day or so is not uncommon, but later from 200 to 500. Of 16 such cases in our series the weight of the kidneys averaged 430 grams (360 to 500), and the cortex averaged 8 mm. (It is interesting to note that the heaviest kidneys were in women.) In these cases the amount varied from 30 to 2,000 c.c., according to the stage of the nephritis. Toward death there may be a diminished or an increased voiding. The specific gravity was normal as a rule, from 1015 to 1017, but in some cases it was from 1023 to 1025 (when the urine was from 300 to 600 c.c.). It is usually of a dark color and cloudy, and blood is nearly always present, as pigment or cells.

Albumin is an almost constant feature, and yet in some severe or fatal cases there may be but traces, and this only on a few days, alternating with periods with none, even to death. As a rule it is not above 1 per cent. In the sediment may always be found red blood cells, mononuclear cells, few polynuclear leucocytes and epithelial cells from the urinary tubules, which are single or in masses, and often very fatty. Among the crystals uric acid and calcium oxalate are found, and hemoglobin, either in amorphous granules or in casts.

In the hemorrhagic form of the disease in our series the red blood cells were remarkably few in number. The leucocytes were very abundant in one case of acute nephritis with multiple abscess.

Casts are present in varying amounts and may be of any form. Epithelial, hyaline and coarsely granular predominate. Blood and leucocyte casts may also be present. As a rule, the number runs parallel to the amount of albumin, yet it varies greatly from day to day, and on some days there may be enormous numbers. In one case of acute hemorrhagic nephritis with areas of complete necrosis the amount of albumin was slight, but the casts, leucocyte and granular, were in large numbers. In one case of general septicemia the albumin was in but traces on certain days, none on others, and yet blood, hyaline and leucocyte casts were found.

In mild cases, and in severe ones as they improve, the urine approaches normal. It is said that the albumin disappears last. In most cases, however, we believe that the casts are found later.

Among our cases of nephritis were 109 of the acute form. Of those patients who recovered 64 were under 45, and 17 were over 45 years of age. Thirteen unsuspected cases were found at autopsy. In eleven cases a diagnosis of acute nephritis was corrected at autopsy, 2 being unsuspected cases of large red kidney, 1 of large white kidney, 6 of subacute nephritis and 2 of the small white kidney. Twenty-six patients were admitted during the first seven days of their illness. In these cases the urinary symptoms were almost parallel with the clinical symptoms and especially with the amount of edema. The urine varied ordinarily from 200 to 300 c.c. for 24 hours, with a high specific gravity, from 1020 to 1030, those with a high specific gravity being in all cases those with much albumin. In 11 of 26 cases this was over 1020 and in 3 cases over 1030. The amount of albumin varied much, being above 1 per cent. in 1 case, above 0.5 per cent. in 6, and in traces in 5. In all of these with traces the specific gravity was under

1018. Casts of all varieties were present—hyaline, granular, epithelial, blood and pus, and waxy in but 1. The cells which were usually present were epithelial, red blood cells and pus cells. During the course of these cases in the hospital the amount of urine increased even above two liters and in 4 cases of the 25 above four liters. The albumin dropped to a trace or to none, and the casts continued, in those previously mentioned, while waxy and fatty casts also appeared. In nearly all cases in which albumin disappeared, the casts continued longer. At the end in those not doing well there was much albumin with many casts. In this series of cases the patients did much better than those admitted later in their disease. There was little difference in the course, for those appearing with traces and those with large amounts of albumin, although the difference was in favor of those with traces. These may have been admitted after the worst was over. In those patients admitted later, for instance between the seventh and fourteenth days, 12 in number, the amount of urine averaged 9.50 c.c., in 4 over 1,500, and in 1, 3 liters. The mean specific gravity was 1015, the average 1018, and the extremes 1003 and 1030. The albumin was constantly present in larger amounts than in the first series. In 6 of the 12 cases there was over 0.5 per cent., and in only 2 were traces present. The casts were hyaline and granular, but sometimes epithelial (in 5) and blood. In one case a shower of casts followed the patient's getting up from bed. In these cases the albumin lasted longer than the casts.

Thirteen patients were admitted during the third week of the disease. Five of these had only traces of albumin; others, much. There were hyaline or hyaline and granular casts in 7 cases (those with fair urine output), epithelial and blood also in the others, in which latter group are the patients with considerably diminished output of urine (in no case over 900 c.c.).

Twenty-one patients were admitted after the third week. These were either on the road to recovery or doing badly as a result of their previous poor condition. The amount of urine varied from 3 to 4 liters in six cases. In some, the amount of albumin was very large, even over 1 per cent. Nine of these patients did poorly and we have the notes of the ultimate recovery of but two. The casts were hyaline alone in 1, hyaline and granular in 6, especially the older patients, epithelial also in 8, blood also in 9, leucocyte in 3, waxy in 2.

SUBACUTE NEPHRITIS. CHRONIC PARENCHYMATOUS NEPHRITIS. CHRONIC DIFFUSE, NON-INDURATIVE NEPHRITIS. LARGE WHITE KIDNEY.

This form of subacute nephritis, which may follow an acute attack or develop without this, is characterized by its subacute course, and often by the large amount of edema and effusions usually present in the serous sacs. It occurs especially in young persons, hard workers in exposed, unhygienic surroundings, and as a result of constitutional diseases, tuberculosis, lues, malaria, especially, also alcohol. The diagnosis is usually easy from the history.

The amount of urine is always diminished, the diminution varying as the edema, and is especially small at death. At the height of the disease it varies from about 250 to 500 c.c., but as the case improves, one may void from 5 to 6 liters of a very dilute urine. The amount also is increased as the edema or the effusions begin to absorb. The reaction is faintly acid, but in some cases is alkaline even on voiding, and in all cases quickly becomes so. This makes a search for casts difficult.

This is the form in which the albumin is greatest in amount, both relatively and absolutely. The amount varies as the specific gravity and seems to bear no relation to the edema. It usually is below 1 per cent., and for months may vary from 0.4 to 0.8 per cent. In cer-

tain cases, however, it is much greater. Cases with 2 per cent. are not rare, and Bartels has reported a case in which the amount varied from 4 to 6 per cent. As the case changes to the chronic indurative form the amount of albumin becomes less and less.

The sediments are much the same as in acute nephritis but it is more common to find coarsely granular, fatty and waxy casts. Red blood cells may practically always be found in especially large numbers in the acute exacerbations. There is little difference between the urine of the white and the mottled kidneys except perhaps that in the latter there are more red blood corpuscles, leucocytes, and fatty cells.

We have studied the reports of a series of 30 cases in which microscopically only the signs of subacute nephritis were present. This is important, since the acute exacerbation of a chronic diffuse nephritis can not clinically be separated from this form. These cases may be roughly divided into those in which there are large, pale kidneys, with considerable fatty and granular degeneration of the cells but with the glomeruli little involved, those with the glomeruli much involved, and the hemorrhagic type. Of the former, of 16 cases in 12 the clinical picture was of severe nephritis. Four accompanied various severe conditions, such as septicemia, tuberculosis, typhoid fever. The kidneys were large, averaging 420 grams in weight (220-580 gms.) The cortex averaged 7 mm. (5 to 10 mm.). The urine, for the most part, was about 500 c.c. in 24 hours, with a specific gravity practically normal. The albumin in 7 cases was present in large amounts, from 0.5 to 1 per cent.; in 5 cases there were but traces. Casts were abundant in 5 cases, hyaline, granular, epithelial, waxy in 4 and fatty in 3. Epithelial, red blood cells, and leucocytes were present. In this form there was a certain disproportion between the amount of albumin and the number of casts in favor of the latter.

In 8 cases the glomerular involvement was very prominent. The kidneys averaged in weight 496 grams and the cortex 9 mm. The amount of urine was slightly greater than in the preceding cases (from 600 to 1,000 c.c.), and the specific gravity about 1020. The amount of albumin was large in 5 cases. Casts were very abundant in 4; in 2 the casts were in great numbers and the albumin was but a trace. No fatty casts were reported in this group.

One would expect that a glomerular involvement would affect particularly the amount of albumin, the tubular involvement especially the number of casts, and while in general this may be true, clinically it is of little importance since the two anatomic conditions are always present and variations are but slight.

Hemorrhagic Form.—Of the 9 cases showing this form of nephritis, in five it was part of some general disease. The kidneys averaged 465 grams. The amount of urine was normal, the specific gravity low. Albumin was present but in traces as a rule. Few casts were present but of all varieties, and in one case with but a trace of albumin, many casts.

CASES OF CHRONIC NEPHRITIS WITHOUT AUTOPSY.

These were cases of a subacute or chronic nephritis with very acute symptoms, much edema, and effusion.

It is impossible to say whether these cases were acute exacerbations of a chronic nephritis or a subacute form. We have therefore merely divided them into two groups, those under 40 (in this group a majority of the subacute cases should occur) and those above 40 years of age.

Of the patients under 40 years of age there were 129. Of these 70 could give no cause, in 10 it seemed to follow malaria, 14 exposure to cold, and 6 grippe. The others followed a variety of diseases.

There were 61 cases with much edema. In 49, or 80 per cent., the urine presented the following features:

it was normal in amount and specific gravity; albumin large in amount, in 20 per cent. over 1 per cent., in 4 cases over 2, and 1 case 3.2 per cent, The casts were in enormous numbers—hyaline, granular, epithelial, fatty, waxy, pus, and blood, in all cases in number out of proportion to the amount of albumin. Among the cells are always found renal epithelium, blood, and pus. In 2 cases cholesterin crystals were found.

In 11 of the 61 cases albumin was present in but traces, and in 1 case none yet many casts.

Of the cases with little edema there were 68 patients who left the ward improved; in 44 per cent. of these the urine presented exactly the same features as the 49 cases above described. Of the rest, in 38 but a trace of albumin was present, in 3 above 1 per cent. Of these in 15 per cent. of the cases the casts disappeared before the albumin and the disproportion was not so great between the two. Yet the relation between the two must depend on the nature of the process, and not its chronicity, since in exactly the same percentage of the cases with a history of less than 6 months' illness did the casts disappear before the albumin as in the much more chronic cases. In this group were also 10 fatal cases. Of these, in 3 there was but a trace or no albumin at the end, in 7 cases more than 0.2 per cent., in 1 case 1.1 per cent.

Subacute Nephritis (or Acute Exacerbations) in Patients Over 40 Years Old.—Of these, excepting the fatal, there were 45 cases. In 28, the first symptom had occurred within six months of admission; in 7, between 6 and 12 months, and in 10, anywhere from 1 to 35 years. No clinical division of this group was possible, hence we group them according to the urine into the following groups:

Cases with a trace of albumin, the amount and specific gravity practically normal; albumin but a trace, and casts only hyaline and granular; cases with a measurable amount, but under 0.2 per cent.; the casts were of many varieties, hyaline, granular, epithelial,

waxy and blood casts were found; and cases, in which there was still more albumin, all kinds of casts were present, including many epithelial, fatty and waxy. In these last cases the casts were sometimes in the background, while in 1 case of leutic nephritis with 2.2 per cent. in many records no casts were found at all. In other cases, all kinds and many were found. In addition to these, there were 10 fatal cases; 4 of the patients died with traces of albumin; of these 1 had enormous numbers of casts, all granular and hyaline; 2 had few casts. In 4 the albumin was greater in amount, the casts either hyaline or hyaline and granular, and in 2 cases none. In 2 cases there was over 0.2 per cent. albumin, with hyaline and granular casts.

CHRONIC INTERSTITIAL NEPHRITIS.

Chronic interstitial nephritis, even in advanced cases is marked by its very insidious course. Its only symptom may be a slight albuminuria, and this may be absent over long periods. Later the albumin becomes permanent, casts appear, and later polyuria. The urine is increased slightly at first, but in a well-developed case from 2 to 3 liters are voided daily, and rarely even as high as 12. On the other hand the amount may at times sink to normal and even under. It is pale, clear, definitely acid, and of a specific gravity which is constantly between 1010 and 1005. This low specific gravity of a morning urine is always significant of this condition. The molecular concentration is diminished. The albumin seldom rises above .05 per cent. and usually is in mere traces. Casts are few. They are often absent in the morning voiding and may, indeed, be present only after a day of unusual exercise, or an especially hearty meal or some unusual excitement.

Of arteriosclerotic kidneys the urine contains the faint trace of albumin which occurs late and is often intermittent. Cases of the so-called contracted kidneys, particularly those albumin-free, belong here. The sedi-

ment is scanty and difficult to find. The urine should be centrifugalized and search made in large amounts of urine. After a long search but one or two casts may be found, usually hyaline, although sometimes a finely granular. Renal epithelium is sometimes found, a few leucocytes, rarely a red cell, and yet many after over-exertion, etc. Uric acid and calcium oxalate crystals are common.

During acute exacerbations the urine often loses this character entirely, and it may be very difficult to distinguish the condition from acute nephritis. It is well to examine the morning and the evening urines separately, and especially after a day with a particularly hearty meal or severe exercise During the whole course the urine in this condition resembles that found in other conditions so nearly that the clinical history and the physical examination of the patient can not be dispensed with. The urine alone, for instance, may resemble the acute or the subacute nephritis during convalescence, waxy kidney, and the cyclic, or the so-called physiologic, albuminurias.

A division of this form into groups is exceedingly difficult; in fact, the size and color of the kidney is almost the only criterion since in nearly every case all its histologic elements are affected by degenerative, inflammatory and regenerative processes. This form of nephritis is of almost physiologic occurrence in every elderly person, the kidney becoming old with the rest of the body, and therefore slightly sclerotic. If the process, however, is simply sclerosis there should be no urinary symptoms, and hence such cases are not suspected before the autopsy. As a result of hard work, worry, various diseases as gout and lues, and certain poisons like lead and alcohol, there is degeneration of the epithelial elements and inflammation, resulting in a new growth of connective tissue, which may be general or focal, subcortical or periglomerular. The kidney be-

comes hard and firm, diminishes in size, and finally may be but a remnant of an organ.

In some cases contracted kidneys are found at autopsy which could not possibly have been recognized clinically from the urine. These show that a nephritis limited to foci can heal. In all such cases if it be the sclerotic process which predominates there may be practically no urinary symptoms, and at autopsy kidneys of surprisingly small size have been found. Other cases are the result of a preceding acute or subacute nephritis. The only classification which can be made, apart from the weight of the kidney and the thickness of its cortex, is according to color, hence the division into red and white kidneys, the red kidneys being the result particularly of arteriosclerosis as a primary factor. The red kidneys are large, firm, beefy, the sclerosis is considerable and yet the size of the kidney is seldom as much diminished as in the white form.

CHRONIC INDURATIVE (INTERSTITIAL) NEPHRITIS. CHRONIC DIFFUSE NEPHRITIS. WHITE KIDNEY.

Of these we have had 174 cases with autopsy. In all the following pages by weight is meant that of both kidneys.

Kidneys Over 300 Grams in Weight.—In this group are 79 cases. Of these, in 38 there was no acute renal process. The condition in some was found accidentally at autopsy on a patient dying of some other disease. The weight of these kidneys averaged 330 grams, and the cortex averaged 6 mm.

The amount of urine was practically normal, as also the specific gravity. Albumin was present in traces as a rule (26 cases). In 10 cases, however, it was present in abundance. In 5 cases on some days there would be a trace of albumin, on other days none, while in 1 case no albumin was ever found.

The casts were hyaline and granular, very rarely fatty and epithelial. In 16 cases no casts were ever found.

We would emphasize the fact that 5 of these 16 were cases of carcinoma, 3 of arteriosclerosis. In 7 cases the casts were in large number. In the sediment, also, were leucocytes, epithelial cells and red blood corpuscles. In the former admissions or at the entrance to the hospital it is the rule that neither casts nor albumin were present or but a trace of albumin without casts.

In 41 cases the kidneys showed also an acute process, in some only a fatty or a parenchymatous degeneration. The average weight was 380 grams; in one case, and that a woman, 720. The cortex averaged 7 mm. Much albumin and many casts were present in 5 cases; a trace of albumin with many casts in 2, with few casts in 14, with none in 11. No albumin but casts were found in 4, and neither albumin nor casts in 2. One of these cases is interesting, since it was of pulmonary tuberculosis with extreme parenchymatous renal degeneration; the urine of the 24 hours preceding death, however, contained neither albumin nor casts. The other was a case of septicemia. The casts were hyaline and granular, in some epithelial, blood or pus.

In 4 cases the acute element was shown by the hemorrhages present.

There were 18 cases in which there was considerable edema and in which the symptoms of nephritis were prominent. These kidneys averaged 390 grams in weight; the cortex measured 6 mm. Here also the amount of urine was practically normal, the specific gravity rather low from 1006 to 1018. The albumin was present in a trace in 7 cases, much in 5. Casts were few as a rule, the most were hyaline and granular, but there were some fatty and waxy casts. Red blood cells, leucocytes, and epithelial cells were also present. In 7 such cases without edema, with a clinical diagnosis of nephritis, the urinary symptoms were practically the same as of those with much edema.

There were 4 cases in which the hyaline degeneration of the epithelial cells was a striking point. It is inter-

esting to note that in one such case casts were never present, but there was much albumin. In one case there were a great many waxy casts and few other forms. In a third case there was much albumin, with granular and hyaline casts, while in a fourth there was only a trace of albumin and no casts.

Kidneys Weighing from 200 to 300 Grams.—There were 57 such cases. Among them was an interesting group of 7 cases accompanying malignant disease. The average weight of these 7 pairs of kidneys was 220 grams; the cortex averaged 6 mm. The urine, both in amount and specific gravity, was practically normal. In all these cases albumin was present if at all, in traces, and in 4 cases it was present only at times, while casts were remarkably few; in 3 cases none were found. The others showed only hyaline and granular cases. In one case, however, there were very many hyalines and granulars; in another on one occasion none, on another many granulars. In this group, therefore, the casts were absent or present in large numbers. In 2 cases with very fat cortices there were no casts.

Tuberculosis: There were six cases; the average weight of the kidney was 257 grams; cortex was 6 mm. thick. Here also only traces of albumin were present in 3, none in 2, and casts few or none. There were few casts in 1, none in 4 cases. In 1 case some time before death many casts had been found. In all only hyaline and granular casts were found.

In 18 cases the nephritis was either an accidental discovery or accompanied some more important condition. The average weight of the kidneys was 260 grams; the cortex measured 5 mm. The amount and specific gravity of the urine were practically normal. The albumin in 10 cases was present in a trace, in 5 cases in abundance, while in 3 none was found. Hyaline, granular, epithelial, pus and waxy casts were found in these cases and mixed casts were common.

In 4 cases no casts were found; in a case of hemo-

philia there was neither albumin nor casts; in 2 cases with very fatty kidneys much albumin and many casts were present; in another case running a slight fever much albumin and many hyaline and granular casts were found.

In this group, further, were 25 cases with definite symptoms of nephritis. In these cases the average weight of the kidneys was about 260 grams, and the cortex measured from 4 to 5 mm. in thickness. The urine was practically normal in amount and specific gravity, although there was a tendency for the latter to be below normal. The albumin varied much, from a trace to even 0.5 per cent. and was present in all cases. The casts were of all varieties, the most hyaline and granular, in two cases there were many; waxy casts were found in 3 and epithelial in 1. As a rule, the casts were few in number; in 4 cases they were many. These cases gave a long history of nephritis. Many of these patients were in the hospital on several occasions. There was a remarkable discrepancy between the amount of albumin and the number of casts.

Kidneys of from 150 to 200 Grams in Weight.—Of these 30 cases, in 7 the average combined weight was 180 grams, and the cortex from 2 to 5 mm. The amount of urine was normal, but the specific gravity in all cases was slightly low—from 1008 to 1014. Albumin was present in traces, if at all. The casts were few in number—hyaline and granular, or none. These 7 cases were not diagnosed clinically as nephritis.

In 11 cases with edema and in 11 cases without edema the clinical diagnosis was nephritis. The weight of the kidneys averaged 180 grams. In both groups, the cortex averaged 3 mm. The amount of the urine of both groups was normal; the specific gravity low, as a rule, in some cases normal. The amount of albumin varied greatly, from a trace to 0.7 per cent. Casts were present in great variety and numbers; in some cases there were many and all forms; in some none. Red blood cells

were commonly present. It should be borne in mind that all these cases mentioned with a clinical diagnosis of nephritis were acute exacerbations of a chronic form. From the urine alone, however, such a diagnosis could not be made.

In those cases with much edema the casts were abundant in 3 cases, very few in 3, while in those with little edema none were found in 5 cases and many in but one. In this latter group only hyaline and granular casts were mentioned; in the former all varieties in some cases.

Kidneys Below 150 Grams in Weight.—Of these, there were 8 cases; the sum of both kidneys averaging 180 grams and the cortex measuring from 2 to 4 mm. The urine was either normal in amount or slightly diminished. The specific gravity was often low, but sometimes normal. The amount of albumin was a trace in 6 cases and a larger amount in 2. The casts were chiefly hyaline and granular, with epithelial in 3 cases and waxy in 2. In 4 cases casts were very scanty and at times not found.

Such were the terminal urinary features of cases which commonly pass as small contracted kidney and of which the classical urinary symptoms are quite different from the above. Polyuria is one of the first complaints; the patient rises at night several times to void urine of a light yellow color, with no gross sediment; the specific gravity is constantly low, varying from 1005 to 1012. Albumin is present in traces with intermissions of none for periods of from a few days to months. In the sediment very few cells and casts are found. For the latter it may be necessary to centrifugalize and to examine a large amount. The casts will be of a hyaline or finely granular nature. It is interesting to note how many of these specimens of urine have a few red blood cells in the sediment. Functionally the kidney is almost perfect. Later, however, and this includes all the cases mentioned, the kidneys are the seat of an acute process,

the amount of urine diminishes, the specific gravity rises and albumin and sediment increase so that from the urine alone one would suspect an acute exacerbation of an acute nephritis in a kidney of much greater weight than he finds at autopsy. In certain other cases, however, in which it is not the renal symptoms which predominate at death, the amount of urine may grow larger and larger until a permanent catheter is necessary, the patient dying in uremia.

In 7 of these cases hyalin was present in the capillaries. In one, with combined weight 155 grams, albumin was 0.3 per cent., casts small in number, and when present hyaline and granular. In one of 220 grams' weight the albumin was 1.2 per cent. and the casts in large numbers, hyaline, granular and especially waxy and fatty.

CHRONIC INDURATIVE NEPHRITIS. RED KIDNEY. ARTERIOSCLEROTIC KIDNEY.

Of the 104 cases studied, the combined kidneys weighed above 500 grams in 12 per cent.; from 400 to 500 in 18; from 300 to 400 in 31; from 200 to 300 in 33, and below 200 in 6 per cent. It is thus seen that these kidneys averaged much larger than the white kidney just described.

Kidneys Weighing Over 300 Grams.—In 46 of these cases the nephritis formed no part of the clinical picture and was not even mentioned in the diagnosis. The average weight of these kidneys was 412 grams, the cortex measuring from 4 to 7 mm. The urine was normal in amount and specific gravity. Albumin was present but in traces, if at all; the casts were few, absent in 18 cases at times, at least, yet in 10 cases hyaline and granular and epithelial casts were abundant at times. On some days many were present. In 8 per cent. albumin was absent for a time at least. While there is a rough parallelism between casts and albumin, the former is more variable.

In 19 cases the diagnosis was nephritis. The kidneys averaged 390 grams in weight; the cortex measured from about 4 to 8 mm.; amount and specific gravity were normal. The albumin was often of fairly large amount, even 0.4 per cent. In 9 cases there was only a trace. The casts were almost constant (yet absent at times in 4 cases), or hyaline and granular.

Kidneys Weighing from 250 to 300 Grams.—In 23 cases the symptoms of nephritis were the subordinate element, in 16 cases the predominating element. The urine was practically the same in both groups. It is interesting to note, however, that the specific gravity ran a little lower than in the preceding group. The albumin varied in amount, and casts of all varieties were present, sometimes in enormous numbers. In the first mentioned group, however, they were often few and only granular and hyaline, while in the latter group waxy and epithelial casts occurred.

Kidneys Under 250 Grams in Weight.—Of the 22 cases in this group in 14 the nephritis was unimportant, while the other 8 were acute exacerbations. The kidneys averaged about 210 grams in combined weight and the cortex measured from 3 to 5 mm. The amount of urine was in all practically normal, also its specific gravity. Albumin was present in practically all cases, usually as a trace, but sometimes a fair amount. The casts were few as a rule, but often many granular and hyaline, and sometimes waxy (in 4), epithelial (in 4), and fatty (in 1) were found. Even in the smallest kidneys the urinary condition was not very similar to that of the small white kidney.

In all these cases an interesting feature is the fact that at the beginning of their admissions or in their previous admission, even back for several years, albumin and casts were practically always present. It will be remembered that in the white variety both albumin and casts were almost a terminal event.

CASES OF CHRONIC NEPHRITIS. NO AUTOPSY.

As is easily seen from the study of cases with autopsy, the condition of the kidney can hardly be suspected from the urine alone. We shall group the following cases by their clinical features.

(1) Chronic Nephritis.—In some cases there were no acute symptoms, except perhaps a slight edema. Such are cases especially associated with advanced arteriosclerosis or cardiac disease, which dominates the clinical picture. Of 126 such cases 36 patients died. Of the 90 who left the hospital, in 70 the urine was of normal amount, specific gravity almost normal perhaps slightly lowered, varying inversely as the amount, albumin a trace, often disappearing while in the hospital. The casts were almost all hyaline and granular, and in case the albumin or the casts disappeared while under observation it was in 75 per cent. of the cases the latter. We wish to emphasize this point. In 20 per cent. of these cases more than a trace of albumin was present, and even 1 gram per mille. Very rarely epithelial blood and waxy casts were seen. There was an occasional renal epithelial cell or blood corpuscles and leucocytes found.

Of these 36 fatal cases, on admission the patients presented the following features: In 9 there was a trace of albumin and in 3 none. The casts were hyaline and granular, and in 1 case a few epithelial were found. In 3 cases without albumin or casts at first, the casts appeared later. In 10 cases there was a measureable amount of albumin, as high as 0.2 per cent. In 3 of these no casts were found; in the others granular, hyaline and sometimes epithelial were present. In 9 cases there was over 0.2 per cent. albumin, and, in addition to hyaline and granular, also waxy casts. Of these cases at death the albumin was present in 12 cases in traces. In 4 of these it had diminished toward the end. Casts were hyaline, granular or none, and in any case only a few in

number. In 14 cases the albumin at death was measurable but under 0.2 per cent. It had diminished in 3 of these cases and had increased in 2. The casts were few in number, hyaline, granular and in 1 waxy: in 1 case none. In 5 cases there was a final shower of casts. At this time the casts were almost all hyaline and granular, and a rare epithelial and fatty cast. In 8 cases the albumin was over 0.2 per cent., in 1 case 0.7 per cent. The casts were present in vast numbers in 3, yet here they were almost all hyaline and granular, with a few epithelial. This lack of variety of the casts, despite their immense number, would seem to indicate that this shower was due chiefly to vasomotor changes in the kidney preceding death and not to an intensification of the nephritic process.

(2) Chronic nephritis in arteriosclerotic or cardiac cases in which the patients had acute symptoms on admission, especially edema. Of these there were 57, 13 of whom died. Of the other 44 cases, in 26 the urine was practically the same as described above, except for a polyuria of even 6 or 8 liters which often occurred during the absorption of the edema or effusion. This was well marked in 35 per cent. of these cases. In 32 per cent. there was more than a trace of albumin. This often diminished or even disappeared while the patient was in the hospital. Of the 13 fatal cases, at the onset there were traces of albumin in 2, a small but measurable amount in 1, and over 0.2 per cent. in 3. There were large numbers of hyaline and granular casts. Toward death a trace of albumin was found in 4 cases; in 2 of these it had been more. These patients had often very many casts of practically all varieties. In 5 cases with more than a trace there was less than 0.2 per cent. albumin, in some many hyaline and granular casts and in 1 case none. In these cases the casts are a subordinate feature and if numerous there are only hyaline and granular found.

AMYLOID DEGENERATION.

Amyloid degeneration may be superimposed on any form of nephritis of which it really forms no part.

In the majority of cases the condition can not be suspected from the urine alone, although given a case with history and physical signs indicating it and the urinary changes may be well explained. Disregarding the clinical features the urine would suggest on the one hand, when concentrated, chronic passive congestion; on the other, small contracted kidney.

The following is the classical description of the urine: It is increased in amount, is pale, clear, faintly acid, of low specific gravity, from 1005 to 1012, and abundant albumin as a rule, with relatively much globulin, and very few casts. This picture of Traube, however, is rare. The albumin may be little or none and the casts may be numerous. They are often fatty. Waxy casts may occur here, but are not at all distinctive. Renal epithelium is rare; red corpuscles extremely so.

Of the 18 cases of which we have notes, in 9 the nephritic symptoms were the unimportant, and in 9 they were the important features. Nine of the pairs of kidneys weighed more than 400 grams; the smallest weighed 210. The cortex varied in thickness from 6 to 9 mm. The amount of the urine presented nothing peculiar; its specific gravity in the majority of cases (9 cases) was lower than normal and in only 3 did it reach 1020.

The amount of albumin varied, in 5 cases being present but in traces, while in 7 cases there was as much as 0.8 per cent.

The casts varied almost as much; sometimes there were many, sometimes few, in 2 none. In only 2 cases were waxy casts abundant, and there were epithelial casts in but 2. In 1 case with 0.2 per cent. albumin the examinations on six days showed but one cast. In the other cases, as a rule, they were few in number. In one case with 0.9 per cent. of albumin a few hyaline and

granular casts were present on some days, on other days none.

RENAL ATROPHY.

This condition may be due to insufficient blood supply, to cachexia, to the anemias, and especially to advancing age, the senile atrophy. It is never great in amount. Microscopically sclerosed glomeruli are seen, but there is no great increase in connective tissue. The urine is practically normal and without albumin.

UREMIA.

We have abstracted the histories of 96 cases of nephritis with uremia. Of the 54 cases in which the first symptom of the nephritis dated back less than six months 42 patients died. Of the 35 cases with an old history of nephritis 29 patients died. Senator states that the amount of urine is diminished or there is even anuria; rarely does this fail, and more rarely is there polyuria at the onset.

Of 8 cases of terminal uremia the albumin was increased in all. In 1 case of uremia with a trace of albumin on the day before and the day following, on the day of the convulsions there was a large amount with a great many casts.

Of our 21 non-fatal cases thus diagnosed, the urine was at the upper limit of normal in 18 and was much increased in 3 cases. The increase was at certain periods and alternated with smaller amounts. The specific gravity was not over 1010 in 10 cases. There were traces of albumin at times and periods in which none was found; hyaline and granular casts were also present.

SUPPURATIVE NEPHRITIS.

In these cases we found the ordinary symptoms of acute nephritis with albumin of varying amounts, but only a few casts. In the sediment, however, in one case there were a great many red blood cells and leucocytes. In the other cases these seem to have been very few.

ABSCESS OF THE KIDNEY.

In practically all cases there were microscopically pus cells present, although few in number. The albumin was present in but traces, and was often absent. Either no casts were found, or only a few hyaline and granular present occasionally. The reason may be the same as for the absence of albumin, viz., that for days this kidney may excrete nothing.

TUBERCULOSIS.

In all our cases of tuberculosis of the kidney of which we have notes there was a trace of albumin and a few hyaline and granular casts. On one day in one case there were enormous numbers of casts with a trace of albumin, but later the casts were fewer in number.

CONGENITAL CYSTIC KIDNEY.

The urine in this very rare condition may be normal, or may show the picture of the chronic interstitial nephritis with small, contracted kidney. The amount of urine increases and the specific gravity is low, with or without a trace of albumin; often blood cells are found. In our two cases the specific gravity was from 1007 to 1013. Albumin was present only as a trace, but terminally even as high as 1 per cent. was found. In one case, in a great many examinations, but one hyaline cast was ever found; in the other case, with 1 per cent. of albumin, no casts were found. Red blood cells and various epithelial cells were quite constant.

CANCER OF THE KIDNEY.

In 4 patients with cancer metastases in the kidney, in 1 without nephritis there was a trace of albumin, and many hyaline and granular and a few waxy casts with renal epithelium. In another case in which the right kidney was practically destroyed the specific gravity of the urine was from 1017 to 1030, a trace of albumin was present on certain days and no casts at any time. In another case, in which the left kidney was practically gone, there were neither casts nor albumin.

"SHOWERS OF CASTS."

Very interesting events are "showers of casts"; by this we mean the sudden and temporary appearance of large numbers of casts in a urine in which before and after few or none had occurred. The albumin may increase or decrease or remain practically the same.

Wagner gave as reason for pure cylindruria that the casts were formed during a transient albuminuria, remained in the tubules, and were later washed out as urinary excretion improved. This would hardly apply to cases in which a long-continued cylindruria is the important feature, and the albuminuria very transitory, but may explain some of these showers of casts which contain none but the varieties formerly present.

They occurred in 34 of our cases with autopsies, and it is interesting that 28 or 85 per cent of these were cases not diagnosed clinically as nephritis since the renal features seemed subordinate.

These cases were nearly all of slight chronic diffuse nephritis, often with scarcely any symptoms, and the sudden increase in casts meant some sudden disturbing element; perhaps a circulatory change, or the elimination of some irritating body.

The best illustration is Külz' sign of oncoming diabetic coma. Suddenly, within twenty-four hours before coma, there appears a quantity of casts in the urine, chiefly finely granular, perhaps unparalleled in clinical experience, which form a huge gross sediment filling the urine glass even one-sixth, and sometimes without albuminuria.

These casts are of characteristic appearance, with a short, broad, delicate outline, pale, and mostly granular and hyaline, with few other formed elements.[1]

There are two general varieties of this output of casts: those with the sudden appearance of large numbers of the same kind of cast as was previously present, and

1. Domanskij and Reimann: Ztschr. f. Heilk., 1901: Herrick: Amer. Jour. Med. Sc., vol. cxx, 1900.

due perhaps to the washing out of the tubules. This follows a diuresis, due, for instance, to a salt infusion. Since the casts long in the tubules are often waxy, these may appear for the first time.

The other variety has casts of all sorts present, especially those indicating an acute exacerbation of the existing disease.

These showers of casts are usually terminal events. They may be manifestations of an acute terminal process, with increase in albumin and the other elements of an acute nephritis. This was true in 12 cases, 6 of them cardiac and arteriosclerotic patients, one a case of liver cirrhosis, and three febrile cases, typhoid, pneumonia and pleurisy, and two of nephritis and uremia.

Or there may be a final increase of the casts only; this was true of 5 cases, 3 of chronic nephritis and arteriosclerosis, 1 a heart case, 1 a case of cancer.

In 6 cases in the terminal shower casts appeared then for the first time, or at least followed a cast-free period; this was true of a case of gout, in which there were small contracted kidneys, two cases of cancer of the stomach, two of tuberculosis and one of arteriosclerosis with cerebral hemorrhage.

The shower may occur during the course of the disease. Then also it may be an acute exacerbation of nephritis, as in three cases, two of arteriosclerosis, one of typhoid fever with suppurative nephritis. In a case of thoracic aneurism and one of tertiary lues, there was only a trace of albumin present.

The cylindruria may introduce an acute process and then diminish as the albumin appears; as in a case of chronic parenchymatous nephritis. Or the albumin may appear even a month later, as in a case of cancer of the stomach.

If the shower follows a diuresis to any cause, as a salt infusion, the casts probably represent the washing out of casts resting in the tubules, and in nature are

similar to those previously present. In one of our cases it followed the man's rising from bed.

In three cases no casts were present immediately before nor after. One was a case of multiple renal abscess and two were cardiovascular cases.

In 25 other cases the casts were out of all proportion to the albumin, which was in some cases absent for a time or during the entire stay in the hospital; in others at most there was but a trace. The general conditions were: Typhoid, 1; pneumonia, 3; pyemia, 1; malaria, 1; sarcoma, 2; tuberculosis, 4; endocarditis, 3; dysentery, 1; cardiac disease, 4; cirrhosis of liver, 3; septicemia, 1; cerebral tumor, 1.

The renal condition was: Acute nephritis, 1; acute hemorrhagic nephritis, 2; glomerular nephritis, 1; subacute nephritis with infarcts, 1; fatty kidneys, 5; congestion, 2; cloudy swelling, 3; metastatic abscess of kidney 1; tuberculosis of kidney, 1. The others were cases of chronic diffuse nephritis; only three of these cases were clinically nephritis.

In 39 of other cases a small amount of albumin was present, but no casts or only an occasional one.

The clinical diagnosis was: Cardiac and arterial sclerosis, 6; cancer of the stomach, 4; thoracic aneurism, 1; tuberculosis, 7; cirrhosis of liver, 2; chronic diffuse nephritis, 3; leprosy, 1; acute peritonitis, 1; acute lobar pneumonia, 6; pernicious anemia, 2; septicemia, 1; congenital cystic kidney, 1; pyelonephritis, 1; typhoid, 2; diabetes mellitus, 1.

The renal diagnosis was: Chronic diffuse nephritis, 24; fatty degeneration, 7; fatty and cloudy degeneration, 1; extreme cloudy swelling, 2; subacute nephritis, 1; acute nephritis, 2; chronic passive congestion, 1; amyloid disease, 1; congenital cystic kidney, 1.

In 19 cases no casts were present and no albumin.

The clinical diagnosis was: Exophthalmic goiter, 1; Hodgkins disease, 1; tuberculosis, 5; acute lobar pneumonia, 1; lues, 1; colitis, 1; cardiac disease, 2; acro-

megaly, 1; cancer of stomach, 1; chronic bronchitis, 1; diabetes mellitus, 1; hemiplegia, 1.

The renal diagnosis was: Fatty kidney, 3; cloudy swelling, 3; chronic diffuse nephritis, 9; waxy kidney, 1; chronic passive congestion, 1; arteriosclerosis, 2.

OCCURRENCE OF CASTS.

In nephritis the epithelial casts occur wherever the process is at all acute, yet they occur in other conditions not nephritis. Their occurrence suggests the statement formerly made, yet often denied, that the renal epithelium is easily desquamated, as is any mucous surface from a slight "catarrhal irritation."

The coarsely granular casts occur especially in a subacute process; never in transitory processes.

Fatty casts occur especially in conditions with fatty degeneration of the epithelium, hence especially in the large white kidney of subacute or chronic nephritis, and in our experience in malarial nephritis. They occur also in phosphorus and arsenic poisoning. These two forms of casts are of greater significance than the epithelial, yet even they may occur in simple chronic passive congestion.

Blood casts occur in large numbers in acute nephritis or acute exacerbation of a chronic nephritis; in considerable numbers in subacute nephritis, perhaps always, while even in the most chronic cases one is apt to find a hyaline cast with a blood cell attached.

Blood casts occur also in conditions not nephritis, as in circulatory changes in the kidney, after the exertion of athletes, and in cloudy swelling. They occur much oftener than they are reported. Fibrin casts are very rare, and if they occur at all it is in intense hemorrhagic processes. Pus casts (cells attached to hyaline casts) practically always may be found in any acute nephritic process. Casts composed entirely of pus cells occur chiefly in suppurative lesions; but leucocyte casts, both pure and combined, are much more numerous than

suspected; some of them are called epithelial, and most are not recorded. Slight irritations of the kidney cause the output of leucocytes even more frequently than of hyaline casts, as if the first indication of irritation was pus in the urine, then hyaline casts and with them often casts with cells attached (see Gläser, also Lütke).

Waxy casts may occur in amyloid degeneration of the kidney, but not always, and are not best seen there. They are the rarest form, and occur chiefly in subacute nephritis, anywhere where coarsely granular casts occur, never in transitory conditions. In our 36 cases in which they occurred, all but three were cases of pronounced nephritis, chiefly chronic. The suggestion that these casts occur best after a considerable stasis in the tubules is relieved, that is, that they are only very condensed hyaline casts or granular casts which have undergone this metamorphosis, is borne out by the facts that we have seen the most brilliant pictures in cases after decapsulation of the kidney, also in the urine found in the bladder just at death; also that in sections the casts in closed tubules are waxy.

Finely granular casts occur in all cases of chronic nephritis, and are of much greater importance than hyaline.

The truly hyaline casts occur in any condition in which albumin might be expected, always in nephritis, and in the simplest, most transitory circulatory disturbances. They may be the only cast present in the severest form of nephritis, the chronic interstitial with uremia. No better illustration than this is necessary to show how little can be concluded from the presence of hyaline casts alone.

That great group of casts called hyaline, which resemble slightly the waxy, occurs in all forms of nephritis.

The hyaline casts occur oftenest; they may mean little or nothing, but they are the first to appear in a pathologic process, and the only ones in some most seri-

ous conditions, therefore they must not be overlooked. If but one form of cast is present, it is always the hyaline; when two, hyaline and finely granular. Hyaline casts are always present when any are. Epithelial, coarsely granular, and fatty may occur one or all, but always with hyalines, although the latter may be rather in the background; the same is to be said for leucocyte and blood casts.

CASTS IN NEPHRITIS.

In nephritis the casts run roughly parallel to the albumin; in acute nephritis there are many, in the severe subacute form most, in the small contracted kidney fewest. In all these conditions it is not the lesion as a whole which controls the cylindruria, but rather more the acute element, hence the urinary picture is often the same in the acute exacerbations of chronic interstitial nephritis as in acute inflammation of an otherwise normal kidney; that is, the process, not the disease. The urinary picture we see in the ward is not as a rule the typical one, especially for the cylindruria of almost normal men. For these, the reports of insurance companies are much more valuable, or those of the examination boards for the Army or Navy.

When the individual is admitted to the hospital it is usually with an exaggeration of the renal condition, hence the condition is more that of an acute process which levels all cases to an almost uniform standard.

In the very acute nephritis one sees many hyaline, granular, epithelial, blood and leucocyte casts. In a case in which improvement is rapid, hyaline and granular casts are found; these diminish rapidly in number, then disappear.

If the case becomes subacute, with a large white kidney and with much degenerated epithelial cells, the hyaline, epithelial and bloody casts continue, but in less numbers, and coarsely granular, fatty and waxy casts appear. Then casts are present in greatest numbers.

If the case goes on to chronic nephritis soon hyaline

and finely granular casts will be found in varying numbers, which will diminish as the case becomes still more chronic, till in the urine of a small contracted kidney will be found after long search only a few hyaline casts, and perhaps not these; yet even while few, some blood casts are seen. When the casts are absent, Bard says that the inflammatory process has ceased.

At any time an acute exacerbation may cause the appearance of all the features so far as casts go of an acute nephritis. In amyloid disease few casts are the classic feature.

From one urinary examination alone practically nothing can be learned. All the casts of acute nephritis could be found in the acute exacerbation of a chronic case; and also in conditions which are transitory and leave no scar, as some cases of cloudy swelling, fatty infiltration, and chronic passive congestion showing all the features of acute nephritis. The same is true after severe physical fatigue, as observations on athletes, bicycle riders and foot racers show; also for a few hours after an operation on the kidney.

In the diagnosis of chronic nephritis, "it is not so much the casts, their number or variety which are of as much importance as other urinary features, the specific gravity; e. g., and of greater value than this is the history of the case, and of greatest value the physical examination of the patient, the cardiovascular features, etc." (Osler).

NEPHRITIS WITHOUT CASTS.

In cases of very chronic interstitial nephritis there may be periods in which the urine is cast-free. The acute inflammatory element in the process has now ceased, but with a slight disturbance they will reappear.

In other cases of nephritis it is more probable that the casts have disappeared because of alkalinity of the urine, etc., than that they were not present.

Treutlein[2] found them constantly absent even in typ-

2. Münch. Med. Wochft., 1903.

ical nephritis in a case of bacilluria. The *Bacterium coli* in the bladder or pelvis of the kidney can cause their disappearance in these cases.

CYLINDRURIA AND NUCLEOALBUMINURIA.

Kossler tried to establish this combination as distinct from albuminuria and cylindruria. These complexes may alternate or the former may precede or succeed the latter. It was present in his cases of "pure cylindruria," in six of which at autopsy only degenerative changes of the epithelium were found, cloudy swelling, fatty degeneration, even necrosis, but no signs of active inflammation. The nucleoalbuminuria and cylindruria of especially epithelial casts occur so parallel that they may be connected; and this might be expected, since nucleoalbumin many think is derived from degenerating cells, and the list of occurrences of nucleoalbumin are those of pure cylindruria as well.

PURE CYLINDRURIA.

To say that there are cases which, from the first, are pure cylindruria, is absurd, since clinical experience shows how temporary is the albuminuria which sometimes is followed by cylindruria; also the wide difference of opinion as to what constitutes a trace of albumin explains many cases.

Among the more acute cases may be mentioned that one reported by Müller in his study of bicycle racers, in which there were many casts, hyaline, granular and epithelial. Cases of pure cylindruria occur in cases of evidently slight irritation of the kidneys, due to foods as asparagus, radishes; to coffee, mustard; to certain drugs, as alcohol, salicylic acid; in certain diseases, especially valvular heart disease, arteriosclerosis, cancer, certain diseases of the nervous system, inflammatory diseases, acute infections. In these cases the casts are hyaline and granular, but also epithelial.

The observations made by Gläser[3] under v. Jaksch's

3. Deutsch. med. Wochft., 1891, p. 1193.

directions are especially interesting. Normal persons from 20 to 30 years of age and not accustomed to much alcohol, and whose urine had been proved normal were given varying but considerable amounts of beer and the centrifugalized urine examined when very fresh. Of 106 persons, the leucocytes were increased in 33, and casts were present in 25. Uric acid and calcium oxalate crystals were other manifestations of the irritation of the kidney by the alcohol. No albumin (careful tests made) was present in any case. In only 6 cases was no effect at all evident.

Of the 25 persons with casts, hyaline and leucocyte casts especially were found in 9. In 7 the casts were hyaline, with a few leucocytes attached; in 2 the casts were agglomerations of leucocytes. Epithelial casts were present in 9, in 8 mixed epithelial and hyaline were present, and in 1 pure epithelial casts. A few fatty casts were found. The effect lasted about thirty-six hours. In severer cases albumin was also present.

Lüthje[4] found that medical doses of sodium salicylate always affected the kidneys. Thirty-three individuals were examined. The administration of this drug was followed always by the presence of casts and cylindroids, leucocytes, often albumin and often epithelial and red blood cells. The effect lasted from fourteen to twenty-one days. Of 204 urine examinations made in 33 cases, in all casts were found and 96 in albumin also. Sometimes with no albumin were many casts. The casts were more especially hyaline and granular, a few leucocytes and epithelial casts were found, never any waxy casts. He thinks the condition a genuine nephritis.

Türk found pure cylindruria after administration of camphor, arsenic, mercury and tuberculin.

Casts alone are more suspicious of nephritis than is albumin alone, but in both cases it is the chronicity of their presence which is of greatest importance.

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4. Deutsch. Arch. f. klin. Med., vol. lxxvi.

The presence of casts without albumin in nephritis is not rare if one centrifugalize the urine well.

For the past two years we have paid this point particular attention and examined all in the hospital in which this condition was present, and we find that in many cases of transient albuminuria the cylindruria will outlast the albuminuria. This is particularly true in those cases of chronic nephritis to be attributed to a parenchymatous lesion, that is, a case previously acute. In those cases of arteriosclerosis, that is, the degenerative type, we find that the reverse is more common. In cylindruria not due to nephritis the casts are rare and those found are hyaline as a rule.

In chronic interstitial nephritis there are often long periods of pure cylindruria, but the casts very scarce indeed, and chiefly hyaline, perhaps with a few finely granular. Such are the cases originally reported by Mahomet, Millard, Purdy and Gull, cases of arteriosclerotic kidneys "arteriocapillary fibroid nephritis."

A pure cylindruria sometimes occurs instead of an albuminuria under the conditions usually termed physiologic.

Stewart[5] reports a group of six or more cases of a type of nephritis which he thinks wholly distinct from the chronic interstitial form. These cases have the symptoms of marked renal insufficiency. He thinks albumin never is present, but casts always, hyaline casts especially, rarely granular, epithelial in two cases, and waxy casts in one case. The cases have not been examined as yet anatomically.

In 3 of 19 cases of erysipelas casts without albumin were found. In 38 per cent. of these cases casts or albumin, or both, were present (Pollatshek[6]). There were in one case albuminuria and casts during the six days of fever, and then pure cylindruria during the succeeding

5. Amer. Jour. of Med. Sc., Dec. 1893; Med. News, April 14, 1894; Lancet, Sept. 4, 1897.
6. Centralbl. f. inn. Med., No. 20, 1903.

six. The other two cases presented few casts, no albumin.

In cases of eclampsia, casts alone may be present after a very slight transitory albuminuria has disappeared. Tonelli[7] reports such a case in which a woman twelve days after delivery went into sudden coma; a trace of albumin was present, then none; but very many casts, especially hyaline and granular, persisted until recovery. It is claimed that as a rule the reverse is true. Friedenberg[8] in 51 cases of postpartum albuminuria found casts in but 3. In tuberculosis pure cylindruria is not rare. Craandyk found it in 10 of 109 cases. The casts were especially hyaline, about a quarter of them granular, a few showed leucocytes and degenerated epithelial cells attached, and in about one-half the cases a few red blood cells were present as well. Kossler[9] found pure cylindruria in 18 cases of chronic tuberculosis, especially those late in the disease with evident cavity formation and a long period of hectic fever. Some at the end had cachectic edema, none symptoms of amyloid disease. The casts were few or very many and of all forms; especially hyaline and granular, almost always a few epithelial; most hyalines had these cells attached, but there were also pure epithelial casts; there were some coarsely granular casts, also some pus casts, on one or two occasions waxy casts, and in some blood casts were present during a long time even in large numbers, some of them pure; in other cases red cells were attached to hyaline casts. Cylindroids were also present. In some cases the cylindruria was very transitory.

In cases of endocarditis sometimes pure cylindruria is found.

Cylindruria accompanies constipation and diseases causing this (confirmed in animal experiments by Wallerstein). Kobler reported two such cases of chronic constipation, two of acute constipation and one of ap-

7. Centralbl. f. inn. Med., 1898, p. 531
8. Berl. klin. Wochft., 1894, No. 4.
9. Berl. klin. Wochft., 1895, Nos. 14 and 15.

pendicitis. He considers the cause a reflex one causing vasomotor disturbance, hence nutritional disturbance of the epithelium. In other such cases the cylindruria outlasts the albumin. The same is true of various inflammatory troubles of the intestine.

One of the first illustrations given was jaundice due to any cause, which was accompanied in every intense case by albuminuria and cylindruria, or the latter alone. Nothnagel found casts always and albumin in but one-third of the cases. In diabetic coma pure cylindruria may occur.

Pure cylindruria occurs in a group of cases in which circulatory changes seem the only common element, as in valvular heart disease and arteriosclerosis, but more often with such cases is pure albuminuria.

CASTS IN NON-NEPHRITIC PROCESSES.

By non-nephritic is here meant a very temporary condition lasting but a few days or hours and with no sequelæ. The condition, of course, often may be a true nephritis.

In our cases of chronic passive congestion with autopsy, hyaline, granular, epithelial, waxy, fatty and pus casts: all gradations from a few hyalines to the picture of acute nephritis, were found; in acute congestion granular casts were found. In cloudy swelling, hyaline, granular, blood, epithelial and waxy casts were seen. In fatty kidneys, hyaline and granular casts were found. Febrile albuminuria is practically always also cylindruria. These accompany jaundice as long as it lasts; diabetes, anemia, and after the ingestion of many irritating foods. Very temporary disturbances of the kidney may present the picture of acute nephritis. These symptoms are present, with a trace of albumin, in about 50 per cent. of cases of general anesthesia for from twenty-four to forty-eight hours. Brown[10] has described some interesting cases of operations on the kidney, the

10. Johns Hopkins Hosp. Bull., May, 1900.

urine previously normal; the operations were nephropexy or exploratory nephrotomy. On the first day following the operation, casts were present in enormous numbers. There were hyaline or granular, blood or epithelial. The field was simply crowded with them. Considerable albumin was occasionally present. They diminished rapidly in number and in a few days (from two to six) had entirely disappeared. During this time there had been no symptoms of nephritis, no edema and the amount of urine was normal. The most striking feature was the disproportion between the amount of albumin and the number of casts, this being greatly in favor of the latter. There were no later symptoms.

Another very good example is eclampsia, in which the cylindruria and albuminuria are extreme, yet at autopsy (after death due to hemorrhage) the kidneys may be found apparently normal.

The postural orthostatic physiologic albuminuria is practically always accompanied by casts, if one take the trouble to search. Casts occur with albumin after the massage given the kidneys by bimanual palpation. Derring, in the urine of the oarsmen of the Harvard crew, found casts common. After a bicycle race, Müller, in the urine of 8 trained men, found in 7 albumin and casts and in 6 very many casts (these 6 including the albumin-free case). The casts were hyaline, granular and epithelial. They were gone the next day. In another group of twelve, casts were found in seven.

CASTS IN THE URINE OF NORMAL MEN.

That casts could be found in the urine of normal men has been believed by the earlier observers from the time of Henle. The finer changes in the kidney in nephritis were not then well understood, and examinations, such as made by insurance companies, were not practiced, hence these men may not have been strictly normal. Again, at that time, cylindroids were counted as casts, perhaps rightly.

As Osler has emphasized, it is rare to find a normal kidney in a man of over 50 years of age. The high strung, rapid life often shows its effect first on the kidneys and a slight increase of connective tissue, and some atrophied and sclerotic glomeruli are found. The process of senile atrophy alone, however, causes no albumin or casts, although half the renal tissue may have disappeared. It is the inflamed degenerated condition of the still-functioning epithelium.

The statement has not recently been made that casts occur in the case of normal men, and all such are considered as poor risks by insurance companies.

MEANING OF CASTS.

Casts occur wherever albumin might or does occur, but although usually associated, either one may be present without the other. It is safe to say that it is the renal cells which are at fault.

The lesion causing cylindruria may be very slight, very trivial, very temporary—some slight temporary disturbance in renal circulation; malnutrition of the cells, anemia due to any cause; the excretion of any irritating substance. Renal cells are some of the most sensitive in the body. Many think that a few hyaline casts means nothing but the most observers agree that any number, even of hyaline casts, means an irritated condition of the renal cells.

The cast may be a good index of the present state of the cell, whether merely irritated or totally destroyed, but gives absolutely no clue to the process behind that condition of the cell, whether a temporary malnutrition or an acute nephritis or a chronic nephritis with almost entire destruction of the kidney and with impending uremia. In fact, it seems as if the cells of a normal kidney could give a more vigorous demonstration of their disturbed condition by a more brilliant output of casts than could those of a diseased kidney. The latter seem to become accustomed to their condition and form even no casts.

To say that casts and albumin run roughly parallel is hardly correct, since one must distinguish between formation and elimination of casts, perhaps between elimination of the materials for casts and their formation.

Casts, however, are of much importance in following a case of nephritis or other renal disturbance.

For them to be present temporarily and then to disappear entirely means, no matter how alarming their number and variety may have been, a temporary and probably harmless disturbance; for them to continue for days, weeks, or months, no matter how few and how insignificant the onset of the trouble, means chronic nephritis; and for them to remain two years means, it is said, an incurable case.

In a case of nephritis, for the number to diminish and to include hyaline and finely granular casts means a subsidence of the acute process, while the reappearance of the epithelial, coarsely granular and bloody casts means a flare up.

That they precede albumin in certain early cases of nephritis remains to be proved. In scarlet fever, the casts may outlast the albumin, which ceases with the temperature, but in some cases from the first there seems to be only cylindruria, and this ceases with the temperature. In typhoid fever pure cylindruria is not at all rare and especially that following an albuminuria. The casts may even become more numerous after the albumin stops.

Phosphorus poisoning may produce only casts, and these in abundance, epithelial with the cells at all stages of fatty degeneration, and fatty casts. Casts also occur in acute infections of various sorts, in the cachexia due to cancer, etc., in diseases of the central nervous system, in various lung diseases, as pneumonia and severe bronchitis, in which blood casts may be the prevalent form, and in empyema.

CONCLUSION.

In the preceding pages we have given the experience of this clinic in the field of urinary diagnosis. The microscopic examination of the urine is indispensable, yet only as an aid to physical examination of the patient, for the examination of one specimen of urine will seldom be enough for a diagnosis.

In conclusion, we wish to emphasize the fact that casts alone are no index of the anatomic renal condition. Their most brilliant display is in non-nephritic condition; the most serious conditions in nephritis may be accompanied by few or none.

The more normal the cells the better do they seem to form casts when disturbed; in chronic conditions the cells seem to become accustomed to their condition and to form few casts or none.

The duration of the occurrence of casts is of great importance, and a given case may be well followed by the casts. Epithelial, blood and pus casts are more common and of less significance than is usually supposed.

THE RELATION OF THE KIDNEYS TO ECLAMPSIA.

PHILIP KING BROWN, M.D.
SAN FRANCISCO.

The sources of my information for this paper are:

1. Statistics from hospitals and private sources on eclampsia and kidney conditions.
2. The literature on eclampsia and metabolism.
3. Personal observations on urea elimination in pathologic conditions of pregnancy.
4. Experiments on the muscular irritability of pregnant and non-pregnant animals.

From the 54,010 records of births in which I could get at least a few important data concerning the frequency of eclampsia in cases of nephritis, renal irritation and toxemia, and the frequency of these conditions without eclampsia, the following facts are shown:

The proportion of eclamptics to births is 1 in 105 cases.

Eighteen and two-tenths per cent. of the eclamptics whose urine was examined just before or after convulsions showed only evidences of "renal irritation" in the urine.

Eighty-one and eight-tenths per cent. showed "nephritis" under the same conditions. "Nephritis" was defined on the circular sent to physicians and hospitals seeking information, so as to include cases showing 0.1 per cent. of albumin and casts, or less marked urinary findings with marked edema of the body. "Renal irritation" included cases with no edema and less marked urinary findings, while "toxemia" included the cases of

TABLE 1.

Figures furnished by hospital or physician.	Total Births.	Eclampsia Cases.			Eclam. Cases no Previous Ur'n Ex			Eclam. Cases Sh'w'ng Before Attack.				Non-Eclam. Cases Showing.				Thre't-ened toxe'ia edema or both		
		Primiparæ.	Multiparæ.	Unclassified.	Later Nephritis.	Renal Irr'tion.	Unclassified.	Nephritis.	Renal Irr'tion.	Unclassified.	Eclampsia cases urine negative before attack.	Nephritis.	Renal Irr'tion.	Toxe. without renal sympt.	Unclassified.	With nephritis	Renal Irr'tion.	Unclassified.
New Engla'd hos., 10 yrs..	2307	19	10	..	5	0	..	23	1	..	..	13	36	4	..	1	4	
Lynn hospital, 10 yrs....	413	10	6	.	..	..	12	2	2	..	..	3	0	1	..			
St. Eliz. hos. Bost., 10 yrs.	680	5	3	..	5	..	..	1	0	..	..	10	3	1	..	2	1	
Mass. homeopathic, 10 yrs.	1497	12	5	..	8	2	..	4	1	..	..	8	3	2	..	1	1	
Bost. Lying In, 10 yrs.....	23521	102	64	..	82	8	..	25	15	..	4	18	7	7	..	22	6	
Worcester city hospital	1900	37	12	..	20	9	..	17	3	..	..	22	7	5	..	4	3	
Colum. hosp. Wash'g. D.C.	3014	34	11	..	..	..	26	9	10	..	..							
B. C. Hirst, Philad'lphia	7500*	..	..	64														
A. L. Smith, Montreal....	1400*	7	1	..	..	..	..	8	..	..	..	10	10					
Johns Hopkins, Balt....	1819	..	..	44	..	..	38	6	..	..	1	10	..	..	655	18	6	
J. B. DeLee, Chicago.....	7000*	..	.	44	..	..	9	..	..	35	..	..	..	..	..	..	..	6
C. A. Kirkley, Toledo, Ohio	1100*	3	2	..	4	..	..	1										
Alex. Maternity, Drs. A. Brown & Von Hoffman.†...	1000	7	3	..	..	..	5	5	..	..	..	41	30	2				
F. Crittenton home, San F.	453	5	0	..	..	..	2	3	..	..	..	10	4	1				
S.F. Lying In E. Harrison.	109	0	0	..	..	..	..	..	..	..	..	1	6	2				
Adelaide Brown, S. F.	297	2	2	..	..	..	..	..	..	..	1	9						
Totals	54010	243	119	152	124	19	92	104	32	35	6	148	99	18	655	48	27	6
Totals		514			235			171				920				81		

*More or less. †San Francisco.

TABLE 2.

SUMMARY SHOWING RELATION OF KIDNEY CONDITIONS TO ECLAMPSIA IN CASES WHERE FULL DATA WAS OBTAINED.

Eclamptic cases with nephritis before or after convulsions...	228
Eclamptic cases with renal irritation only before or after convulsions.	51 (18.2%)
	279
Eclamptic cases with nephritis or renal irritation before or after convulsions (data not enough to classify).	127
Eclamptic cases with no record of urinary findings.	108
	514
Non-eclamptic cases with normal urine	10,360
Non-eclamptic cases with "nephritis"	196
Non-eclamptic cases with "renal irritation" only . . .	787 (7%)

headache, vomiting, dim sight or abdominal pain (other than labor pain) near the time of delivery.

Of the non-eclamptic cases in a series in which 10,360 had normal urine, there were 196 cases of nephritis and 767 of renal irritation.

The full table shows the marked variations in the frequency with which these symptoms occur in different hospitals—depending probably on the care with which the urines are examined in each place. The column marked "eclamptics-urine recorded negative before convulsion"—is significant. The 4 cases recorded in the Boston Lying-in figures may possibly be accounted for by the careless work of students who do the out-patient work. The Johns Hopkins case is specially referred to by Dr. Little as a case where the only record of urine examination before the attack was the statement "urine negative." Dr. A. Brown's case was one in which the patient's urine was free from albumin a week before the attack. Immediately following the examination, the patient caught a severe cold and had temperature for several days prior to the eclampsia. The urine was not examined again until after the attack. That albuminuria is a more frequent accompaniment of pregnancy than these figures indicate is well shown by the examinations of Little of Johns Hopkins and of Trautenroth. Their results are shown in Table 3.

This makes it clear that the kidneys show the strain of the pregnancy and labor by an elimination of albumin in practically every case. In a vast majority of the cases there is nothing to show that this strain is significant of more than the similar appearance of traces of albumin and occasionally casts in the normal individual after exercise. Darling has shown that albumin enough to coagulate solid on boiling may result in the urine of a previously normal person from the prolonged strain of a boat race, and that practically all athletes show traces of albumin and casts after prolonged effort, even when accustomed to it.

The albumin may mark a pathologic condition of the kidney arising during pregnancy or the exacerbation of an old kidney lesion. The occurrence of albumin in large amount so constantly with eclampsia suggests a dependence of both on some common cause. Trautenroth has shown that the death of the fetus in utero has stopped a marked albuminuria, and Strumer reports a remarkable case of a seventh pregnancy in a woman who had eclampsia in her second and fourth confinements. Her other pregnancies had been normal. At time of admission the urine was scanty and loaded with albumin, both feet edematous, and she had headaches. A milk diet and 15 grains of thyroid extract a day resulted in the disappearance of all symptoms in 9 days, including the albumin. She left the hospital under protest, but was brought back 11 days later, having just had 3 convulsions.

TABLE 3.

TABLE OF STATISTICS SHOWING FREQUENCY OF ALBUMINURIA IN PREGNANCY WHERE THE SUBJECT WAS RECEIVING SPECIAL INVESTIGATION.

Urine in	Pregnancy.		Labor.	
Cases , ...	Little (Johns Hopkins,) 715	Trautenroth, 100	Little (Johns Hopkins,) 560	Trautenroth. 59
Negative	49.2%	50.5%	37. %	1%
Albumin.	48.8%	45.5%	62. %	99%
Albumin and casts	10.1%	4.0%	18. %	28%
Casts, no albumin	1.9%			

LITTLE (JOHNS HOPKINS) IN SPECIAL SERIES OF 100 CASES.

	Pregnancy.	Labor.
Negative.	54%	10%
Albumin.	46%	89%
Albumin and casts	14%	41%
Casts, no albumin	....	1%

The occurrence of casts far more frequently in the urine of multiparæ than in primiparæ is a strong argument against the renal origin of the eclampsia poison for 80 per cent. of the cases of eclampsia occur in primi-

paræ, according to German statistics, where the prior kidney condition is more favorable. Lange finds also a common extra-renal cause for a number of the phenomena of the toxemia of pregnancy, particularly the albumin. He shows that the ordinary thyroid enlargement during pregnancy disappears under administration of thyroid, increasing again at the cessation of the treatment. In the 133 cases examined for thyroid changes, 3 were doubtful, 108 showed this enlargement, of whom 2 only had albuminuria. One of these was nephritic, and none developed eclampsia. In the remaining 22 where there was no enlargement, 20 had albuminuria, 16 with casts, and 6 of these developed eclampsia. Lange removed one-fifth of the thyroid in 10 pregnant cats; 2 died in coma 23 and 38 days after operation, 3 had convulsions 23 and 25 days after operation. Of these 5, 3 had albuminuria and fatty changes were found at autopsy in the liver and kidneys. No changes were noted in the other 5 cats during the pregnancy, but, on examination after they were killed, similar changes were found in the organs of 3.

The theory on which eclampsia was first held to be dependent on kidney disease was, of course, this association of albumin with the attacks and the similarity of the convulsive seizures in eclampsia to uremic convulsions. I have tried to make it plain that albuminuria is almost the rule in pregnancy, particularly at the time when eclampsia occurs, and that even severe nephritis and extreme albuminurias occur commonly without signs of eclampsia. Renal insufficiency with retention of toxic waste products, increased by the incident of pregnancy, was the explanation which arose from this conception of eclampsia. Urea naturally held the first place as the toxic agent, as it makes up so large a part of tissue waste and was so long associated with uremia as its cause. Because this view still lingers with some few, I have shown on diagrams the extreme variations in the excretion of urea in 3 cases of pregnancy—the

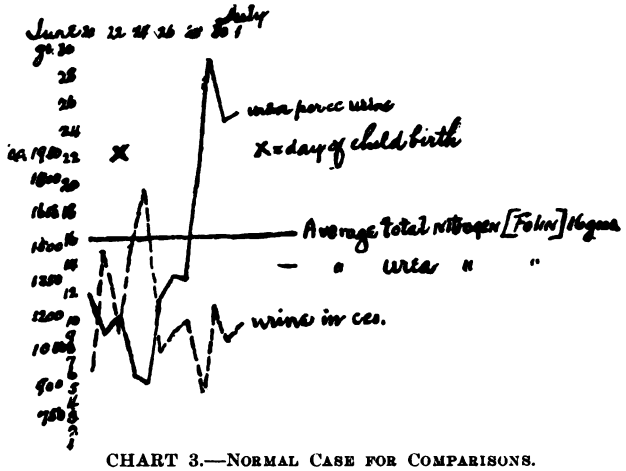


CHART 3.—NORMAL CASE FOR COMPARISONS.

EDITOR'S NOTE: Since this volume went to press, a duplicate of Chart 3, of Case 3, has been secured, allowing this insertion here while the book is being bound. Attention is called to the fact that the cases are mentioned at the top of the page in different order from that followed in detailed account.

first a normal case on full diet for comparison; the second a case of post-scarlatinal nephritis, with marked edema and an amount of albumin varying from 0.1 per cent. to 1.6 per cent. in the last month of pregnancy and the month after it; the third, a case which had had eclampsia in two previous pregnancies and had a trace of albumin with casts in this pregnancy. These last two cases were put to bed on a milk diet while these observations were made. The case which had previously had eclampsia also underwent this régime for three periods of 10 days each during the earlier part of her confinement.

CASE 1.—Mrs. W. B. First pregnancy. Scarlatinal nephritis since childhood. Urine found, early in pregnancy, to contain nearly 0.1 per cent. of albumin, with hyaline, granular and epithelial casts. The patient was brought to San Francisco and kept in bed and a diet given her, consisting solely of milk, for 4½ weeks before her confinement and for nearly a month after it. Chart 1 illustrates the gradual increase in the amount of albumin and the decrease in the urine and the urea, and their extreme variation. It shows further the striking increase in the urine and urea after confinement. That pregnancy is a very severe tax on such a case there is no doubt, although this particular patient bore a second pregnancy two years later without having at any time over 0.1 per cent. of albumin. It is a significant point that on the days of free movements of the bowels, when the urine and urea elimination was low, the percentage of albumin increased strikingly, more than doubling on several occasions.

CASE 2.—Mrs. L. (Chart 2). Has twice had eclampsia at 7 months. Her urine at the beginning of the third pregnancy was found to contain but a minute trace of albumin and a few hyaline and granular casts. For periods of 10 days each, during the middle of the pregnancy, the patient was put to bed on a milk diet amounting to nearly 4 quarts a day, and estimations were made of the functional activity of the kidney in quantity of urine and urea eliminated. For a month before the confinement the patient was kept constantly in bed on the same diet. Here again it is shown that the urea relatively and absolutely diminished steadily up to the day of confinement, after which there was again a striking increase in both the total urea-nitrogen and percentage of urea. The patient was delivered without convulsions.

CASE 3.—Normal case. A normal case is charted for comparison. The patient was on full diet. [The chart of this case has been lost.—ED.]

CHART 1.—PREGNANCY IN CHRONIC PARENCHYMATOUS NEPHRITIS.

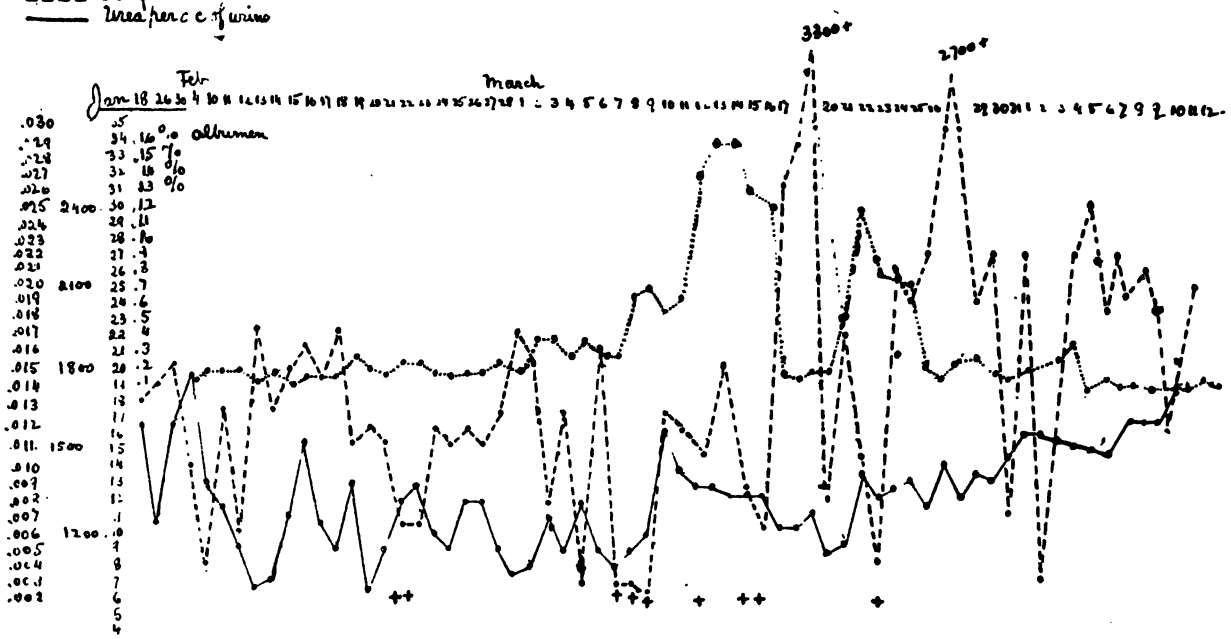
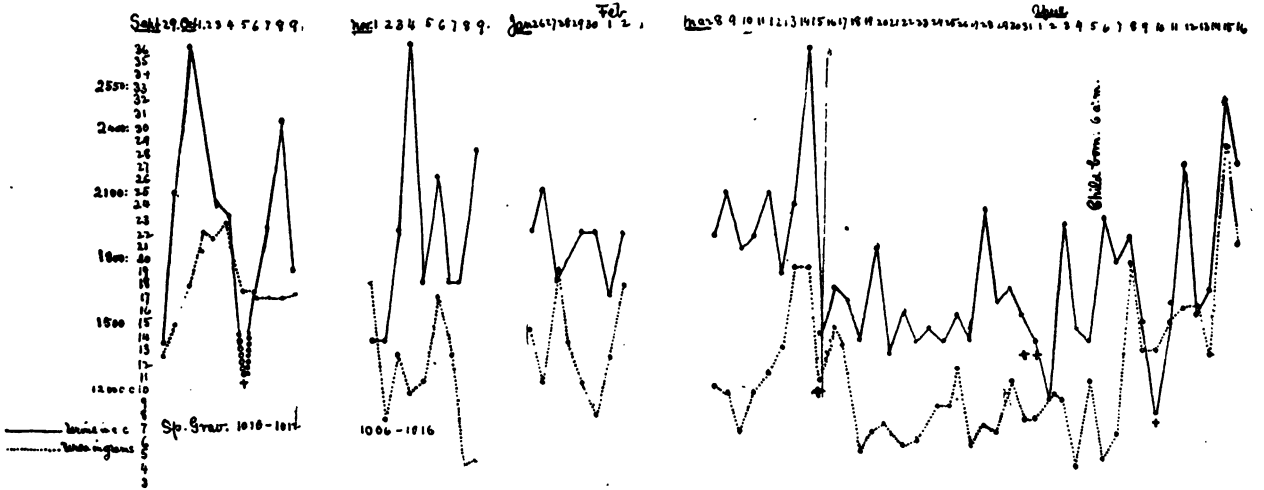


CHART 2.—COURSE OF URINE AND OF UREA IN THIRD PREGNANCY (NORMAL). ECLAMPSIA IN FIRST AND IN SECOND.



Two facts are shown plainly:

1. The urea diminished markedly before confinement, even in the normal case. In the other two cases it was reduced steadily for a month before pregnancy to at least one-third the normal amount and on certain days got as low as three grams. Both of these cases belong to the class of renal insufficiency with retention of urea, but both were confined without convulsive manifestations.

2. They illustrate also the fact that after periods of retention the urea is usually correspondingly increased for a time. This has been shown also in hysterical anurias, where again no convulsions follow the long-continued retention of normal end products.

These three cases will serve to show the extreme fallacy of the urea estimations as evidence of the nitrogenous elimination of the patient, for I have no doubt that the feces during these periods contained a relatively increased amount of nitrogen and the urines themselves contained nitrogenous products in increased quantity in the form of ammonia, kreatinin and uric acid, as has been shown by Folin to be the case in normal persons whenever the urea is diminished. Folin shows, further, in a patient of his that had taken extremely little food for several weeks and no food for five days before the examination he made, that in 24 hours only 125 c.c. of urine was passed, and this contained .85 grams of nitrogen, and that only 14.7 per cent. of this total nitrogen was in the form of urea and 40 per cent. of it was in the form of ammonia. Normally 80 to 85 per cent. of the total nitrogen is in the form of urea and 3 to 5 per cent. of ammonia. Folin quotes a still more interesting case from an analysis by Mörner. This urine contained only 4.4 per cent. of the total nitrogen as urea, with 26.7 per cent. as ammonia. While no particular deductions can be drawn from these cases, they serve to show that the failure of the kidney to eliminate nitrogen in the form of urea has no special significance,

that it depends entirely on diet and the amount of nitrogen eliminated in other ways. In my own experiences I have the records of a case of pernicious anemia with chronic diarrhea where for months not more than 5 ounces of urine were eliminated a day, but where intestinal sand consisting of uric acid was eliminated daily in enormous quantities. This diarrhea had gone on for 20 years, and the woman died of pernicious anemia at the age of 72. So much for the influence of deficient elimination of normal end products. I have not gone into the variations in the quantity of kreatinin ammonia and uric acid, but the conditions under which they increase and decrease in urine in other pathologic states than eclampsia, without causing convulsions, render it most probable that they have nothing to do with this state. It has never been found that any one of them was constantly increased in the blood of eclamptic cases.

Developments in the study of metabolism brought two new theories of eclampsia in which the kidney played some part. The first was that conditions hold in eclampsia whereby normal end products of metabolism were not formed. The liver notably has attracted attention in this particular. Animals in which the Eck fistula had been produced, thus cutting off the function of the liver of destroying or converting certain toxins, died of severe intoxications. None of the known intermediary products, however, have been found to be increased in the circulation or urine, so the theory has little to support it. The second theory supposes from the analogy of B oxybutyric and diacetic acid intoxication in diabetes, which is itself due to a number of causes, that a similar production of abnormal and toxic end products occurs in eclampsia. Bearing out this theory it has been shown definitely that the blood in pregnancy is more toxic than normal, and that this toxicity is further increased in eclampsia. All attempts to show an increased toxicity to the urine have thus far been unconvincing. The source of this increased toxicity of the blood is the pres-

ent point in dispute among the legion of investigators of this subject.

I will not review the subject here, but will state simply that the recent work of Schmorl, Dienst and Liepman calls attention to the fact that the placentæ of eclamptic cases is commonly pathologic; that there are large communicating spaces found in these placentæ; that thrombi of placental cells are frequently found in the maternal veins (although they are found in non-eclamptics also); that the blood of the fetus in eclampsia has a hemolytic action on the maternal blood, and, finally, that serum emulsions from dried placentæ of eclamptics produces death in animals into whom it has been injected, whereas serum from normal placentæ made in the same way is harmless.

Brettaner reports an interesting case bearing on the placental origin of the toxin. A woman of 40 who had had 3 difficult labors, was seized with convulsions without premonitory symptoms at full term. Two children were born, much asphyxiated, but they were resuscitated. The placenta was single; 6 hours later the first child had a convulsion, followed in the next four hours by four more. Eight hours after birth the second child had its first convulsion, and nine others followed rapidly before death ended the attacks. The mother's attacks ceased with the birth of the children.

This case led me to investigate, as far as I could, the question of the size and number of the placentæ in twin pregnancies. It may be a coincidence, but in 3 cases of twin pregnancies, where the mother and at least one child had convulsions, the placenta was single. And in 9 cases obtained from the records of Dr. Adelaide Brown, the only two cases that had no noticeable albumin in the urine during the pregnancy, were cases of double placentæ. In the other seven cases, four had a large amount of albumin, three being regarded as critical cases of the nephritis of pregnancy.

In carrying out the investigations as to whether the nervous system of pregnant women was more responsive to stimuli than non-pregnant women, it occurred to me that the experiments of Loeb on muscular irritability might be applied with some interest to pregnant animals in the hopes that further light would be thrown on the question of convulsions. Loeb found that if the fresh gastrocnemius of a frog were immersed in a solution of a sodium salt, the muscle will show immediate rhythmic contractions which cease when the muscle is immersed in a solution of calcium chlorid. He showed further that if the nerve alone be put into one of these salt solutions, the muscle begins to twitch in about five minutes and finally gets into tetanus. If the nerve be taken out of the solution, contractions cease. "Although this seems to indicate that the salts or other ions stimulate the nerve directly, it can be shown that they have only increased the irritability of the nerve, for when the nerve is brought in contact with any solid or liquid body the contractions of the muscles will be resumed." In furtherance of this suggestion I undertook the following experiment: An isotonic solution of sodium citrate was injected into the peritoneal cavity of pregnant and non-pregnant guinea-pigs. No convulsions were produced in either set of animals by small doses, but increasing the dose or the addition of a small quantity of barium chlorid to the sodium citrate caused immediate general convulsions in the pregnant animals and frequently death in doses that did not affect non-pregnant pigs, even of smaller size. The details of these experiments will be published later.

SUMMARY.

1. Albumin is present in fully 80 per cent. of normal pregnancies.

2. Albumin and casts are found in at least 30 per cent. of all pregnancies.

3. There is no reason to suppose that the renal condition thus revealed is the cause of eclampsia.

4. That there is some connection, however, between the albuminuria and the extra-renal cause of the eclampsia is likely, in view of the nearly constant association of the two.

5. It has been shown that neither any normal end product nor any known intermediary product of metabolism is the cause of eclampsia.

6. It is reasonable to suppose that deficient thyroid or parathyroid activity plays a part, at least, in some of the cases of eclampsia.

7. There are probably several causal factors to the separate or concomitant action of which eclampsia seems to be due.

8. The most significant experimental work done up to this time points to the fact that in the placenta is formed the toxic substances which probably are responsible for eclampsia.

9. There is good evidence that these same substances are, in all probability, the causes of the headache, edema, abdominal pain, and particularly the albuminuria present in non-eclamptic and non-nephritic cases.

10. The nervous systems of pregnant women are in an abnormally sensitive condition. Their blood has been shown to be abnormally toxic. There is no conclusive proof of an increased or diminished toxicity of the urine.

11. My own experiments have shown that the muscles of pregnant guinea-pigs can be thrown into convulsion more easily than those of non-pregnant animals.

THE DIETETIC TREATMENT OF NEPHRITIS.

F. C. SHATTUCK, M. D.
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So powerless are we directly to influence the kidneys by drugs that diet becomes of prime importance in our efforts to do our best for patients suffering from disablement of these organs, which play so leading a rôle in excretion.

The principle which should guide us may be expressed in one word—rest, provided that we remember that in the living body rest is a relative term. Absolute rest, as evidenced by cessation of the output of the kidneys, means death before many days. By rest we mean here, of course, such limitation of demand as may promote either complete restoration of functional activity, or such measure of it as may be possible, together with maintenance of the same for the longest possible time and without injury to the body as a whole or to its other important constituent parts.

Acute nephritis is of all grades of intensity, varying from a trivial process, the only danger of which is lest it become chronic, to one which totally and suddenly disables the kidneys. It is probably nearly always the result of an infection in which the kidneys may bear the brunt of the poisoning or may participate in a wide-spread disturbance, perhaps early, but more often later, in the course of the disease.

For twenty-five years it was almost universally considered the best practice to give a rigid milk diet in these cases and to force water. Water, of which milk

is, of course, largely composed, was regarded as the best diuretic. Milk, moreover, contains, in an easily assimilable form, every nutritious principle necessary for the maintenance of life. The idea underlying the large ingestion of water was to scour the blocked tubules. But we have learned of late years that in many cases the main trouble lies behind the tubules in the glomeruli, the incapacity of which to filter is, in the acute stage, more likely to be increased than diminished by increasing the blood mass and blood pressure.

Experience teaches us that recovery, often complete and lasting, is the rule in acute nephritis provided that a brief danger period can be tided over. Starvation is, therefore, now considered the best dietetic treatment of acute nephritis, absolute starvation for a few days in the severe cases with very scanty or suppressed urine and edema of rapid onset and growth. In cases of less severity, the kidneys allowing the passage of water and dropsy not increasing, about a quart of milk can be given daily and the needs of the system eked out by cereals and fats in moderate amount. The phosphoric acid in the milk which may be difficult of excretion can be precipitated in the intestine by the addition of small quantities of calcium carbonate, as suggested by von Noorden, who also acutely calls attention to the inconsistency of those who absolutely prohibit alcohol but permit koumyss and matzoon. Moderate quantities of alcohol do no harm, he believes, though he seldom uses it. The quantity of food is to be guaged by the degree of kidney disablement as measured by the amount of urine rather than by the amount of albumin, the state of nutrition of the patient and his gastro-intestinal digestive power, all combined. As convalescence advances the quantity and variety of food should be increased, including proteids. Animal broths are almost the last things to be allowed, containing little of nutritive value but extractives, which are dangerous to those liable to renal intoxication.

From a practical point of view the dietetic manage-

ment of acute nephritis and of acute exacerbations of the chronic forms is essentially the same. The general condition of patients suffering from the latter may not tolerate as complete or prolonged starvation as may be safe in the former.

We have learned in these latter days that our knowledge of the real pathology of nephritis is more limited than we once thought it to be and that consequently our classification of its forms is as unsatisfactory as it is tentative. The clinician who, discouraged by his frequent failure to apply the classification of the pathologist to practice, makes a classification mainly on clinical lines, does not help matters much. For our present purpose, therefore, I shall divide the chronic cases into two classes—those cases with and those without dropsy. The second class is chiefly made up of the arteriosclerotic and other cortically atrophied kidneys in which dropsy is conspicuously absent as long as compensatory left ventricular hypertrophy is present. In cases of chronic nephritis with dropsy, especially if the dropsy is mainly of cardiac origin, limitation of liquids is important as a rule.

As far as diet alone is concerned the chief, if not the sole, difference in the treatment of dropsical and non-dropsical cases lies in the degree of limitation of liquids, including water. In some cases, and in some stage of any case water may be excreted with difficulty by the kidneys and, if the myocardium be at all insufficient, increasing the blood mass merely increases the load of the already overburdened heart.

In the chronic cases we have, as a rule, little hope of true recovery and yet we now and then see such a case as this. A young woman who has had renal albuminuria for more than a year marries. She is cautioned with regard to pregnancy. She nevertheless becomes pregnant before long, passes through it and labor successfully, loses her albuminuria, has a second child and remains absolutely well some years later. In other

cases, apparently of the so-called parenchymatous or diffuse type, we note the maintenance of apparent perfect health in combination with a highly albuminous and cast-rich urine for years and years. Apart from these exceptions, however, our aim must be to enable the patient to tolerate his disease as long and as comfortably as possible. Thoughtful attention must be given to the body as a whole, and its nutrition. What doth it avail a man to gain sound kidneys if he lose his life? This means careful individualization of our cases and the effort in each case to adjust the amount, quality and variety of the food to the needs of that particular case at the given time, according to the stage and intensity of the renal process, the condition of other organs and of the whole organism. The best place for printed diet lists so kindly furnished us by the manufacturers of dietetic preparations for Bright's disease, diabetes, gout and other entities, is the fireplace. The physician should be his own prescriber of food as well as of drugs.

The exercise of that form of common sense which, if the ideal be not obtainable, knows how to recognize and secure the best regimen and mode of life possible for the case in hand is no mean help.

In cases with dropsy, with a strictness largely proportional to the degree thereof, a relatively dry diet is advisable. In the cases of contracted kidney, including the "gouty kidney" of the English, I am inclined to think von Noorden right in his opinion that we have erred in the past in forcing water, even in the absence of dropsy, thereby endangering the compensatory hypertrophy of the left ventricle, on the maintenance of which life often depends more than on the kidneys, to the slow wasting of which the system has a chance to accommodate itself.

It seems to me that the main service which von Noorden has rendered is his cogent advocacy of the limitation of liquids. The pendulum had already begun to

swing away from an exclusive milk diet in chronic cases, at least, before his views became common property in this country. His varied diet with a fair amount of proteid is in all essentials the same as that which I have advised my patients and taught my students to follow for at least fifteen years past. I never could see anything in the ban put on red meat save an ingenious mode of limiting the amount of meat. He who eats no meat save practically the breast of chicken eats very little, and less as time goes on, so weary of it does he become. Is it not better to talk straight as well as to think straight? I have long been in the habit of allowing my chronic nephritics meat of any color they please once a day, with fish or eggs at the other meals. As to amount I believe that the best results are to be attained only by study of the special case. We have all seen cases in which nephritis has been overlooked for some reason or another and which were suffering from too much food of all kinds. But I am sure that I have seen more patients with recognized nephritis suffering from an insufficiency than an excess of proteids. Cooking should be simple. Spices and condiments may be undesirable and their prohibition involves no hardship, at all events. Green vegetables and fresh fruits in their season are almost without exception permissible, nay desirable. The more perishable fruits, such as peaches and berries, which have traveled long distances to market, are apt to be poor things for anybody. Varieties are selected with more reference to their appearance on arrival than to their digestibility or palatability. I note that von Noorden forbids celery. I do not know how things may be now, but when I studied in Germany thirty-odd years ago the only form of celery I ever saw on the table was the root. In this country I have seen only the stalk, which, either in the raw or cooked state, I can not think detrimental to nephritics.

The red meat calls up another fad—that of the avoidance of water with meals. Its true purpose may orig-

inally have been to limit alike food and drink and thus to reduce weight. But many persons have got it into their heads that water between meals is no longer water. The interdiction of red meat and of water with meals may be an easy way for the physician to attain a certain end. But the easy way is not always the best way, and I believe that we serve our patients, humanity and ourselves better if we avoid shibboleths, even if the so doing involves trouble and time.

Many women and some men seem to have nothing better to do than to exchange confidences—if those things can be called confidences which are openly talked of in street cars or in places of public amusement—as to their ailments, their physicians and their remedies. I recall a story which I heard of the late Dr. H. J. Bigelow, the great surgeon. A woman sent for him and talked for more than half an hour without interruption from him. When she had concluded he remarked: "Well, as near as I can find out, you have sent for me to ask whether a remedy which Dr. A. prescribed for Mrs. B. for a complaint which you have not got would be good for you." This woman had the sense to refer the question to her physician. Some have not, but go ahead and take the remedy. The practice of medicine is even to-day more of a black art than it would be if physicians always thought clearly and took the trouble to explain principles broadly to their patients. Of course, our knowledge is most imperfect and we must often base our action on half or quarter truths, even on what is not the truth although we believe it to be such at the time. But let us recognize that a fraction of truth is but a fraction, and bear in mind the saying credited to the late Speaker (Tom) Reed—"People say truth is simple: half truths are simple but the whole truth is the most complicated thing on God's earth."

I have no personal experience with the restriction of salt in the diet of nephritics. The investigations of Vidal, Javal, Lemiérre Kövesi, Róthe-Schultz, Strauss

and others make it certainly desirable that further clinical evidence be acquired as to its value in kidney disease with dropsy. While the reports of the many observers are by no means unanimous, the evidence in favor of a low sodium chlorid allowance is sufficient to make us ask for more light. I am only too conscious of the sketchiness of my remarks on this important subject. The imperfection of our knowledge and the size of the subject render it impossible, for me at least, to qualify or to go into minute detail. Principles are more important and of chief concern to us here.

The leading ones pertaining to the dietetic treatment of nephritis may be stated somewhat as follows:

1. Such control as we may have to-day of nephritis lies in diet and mode of life rather than in drugs.

2. Such drugs as are useful are so in their effect on the general organism or on the heart rather than on the kidneys directly.

3. In all cases of nephritis our broad aim is to spare the kidneys unnecessary work, not forgetting that the urinary is but one of the systems which comprise the body.

4. In acute nephritis, as well as in acute exacerbations of the chronic forms, Doctors Diet and Quiet should work together. Starvation for a few days, proportional to the intensity of the process and the strength of the patient, is the keynote of the dietetic management.

5. In the chronic forms we seek to lengthen and lighten life, an aim often largely within our power of attainment. Especially in the contracted form of kidney disease many years of life, much of the happiness which comes from achievement, days and nights of comfort, may hinge on our skill in adapting sound principles to the particular case and in securing the co-operation of the patient in carrying out the same, persistently, not spasmodically. Dietary restriction should be in the main quantitative rather than qualitative. Alco-

hol in moderation is not necessarily a poison and may be an aid to digestion.

6. The excess of proteid, not proteid in itself, is harmful to the chronically sick kidney.

7. A varied is more likely than a monotonous diet to promote the manufacture of good blood and thus to promote good nutrition of the body in general and of the myocardium in particular.

8. The amount of albumin is in itself no guide as to the extent of dietary restrictions.

DISCUSSION

ON PAPERS OF DRS. STENGEL, EMERSON, BROWN AND SHATTUCK.

Dr. John A. Witherspoon, Nashville, said that for a number of years he has been very much impressed with the reparative and recuperative powers of the kidneys. It has been taught, he said, that the kidneys have but little reparative or recuperative powers and yet many physicians have witnessed the disappearance or subsidence of conditions at the bedside, and of the pathologic findings. Everything must be taken into consideration before the physician makes a positive statement, or gives a positive diagnosis. No man can depend on the clinical findings alone at the bedside. The successful man will have to rely in all his cases largely on what he finds by a comprehensive view of the entire situation. In no character of cases is this more necessary than in the consideration of kidney lesions. Dr. Witherspoon has been impressed with the fact that many men are in too big a hurry and rush through their diagnosis too rapidly. In kidney cases above all the quantity of the urine in the twenty-four hours, with repeated test microscopically and chemically of the urine in many cases will make a diagnosis. One can not jump at conclusions as is often done by the simple finding of albumin and casts. The rapidity with which some men make their diagnoses is to be censured, he said. More time should be taken in the examination of these patients. Many cases diagnosed as Bright's disease are not really that disease at all. Many prognoses would be changed if the cases were watched a sufficient length of time. In the management of the cases one should be able to recognize the danger signals even when the patient is apparently getting along comfortably. The process may be an insidious one or a stormy one, but there are certain things that should serve as danger signals, such as the uremia and evidences of cardiac changes. The heart is responsible for many of the troubles that arise with broken compensation, or when the hypertrophied left ventricle gives away. If the physician early recognized these

danger signals, such as twitching of the muscles, or irregular or dilated pupils, or changes in the quality or quantity of the urine and other signs he would be able to prevent many of the subsequent dangers. Dr. Witherspoon said that medicine plays but a small part in the treatment of disease, and less in the treatment of kidney disease than in any other. In these cases success will depend chiefly on regulation of diet and on the general management.

He believes that many men have been much weakened in their vital resistance and in their muscular powers by improper dieting, resulting in malnutrition, especially such dieting as was prevalent years ago. It is horrible to contemplate. Many of these patients with chronic nephritis may live for years if they are not scared to death. He cautioned against allowing the patient to pay more attention to the taking of medicines than to the sanitary surroundings. He has had patients say to him: "I have missed taking a dose of your medicine," and he really wished that they had.

Dr. W. Ophüls, San Francisco, stated that at the pathological laboratory of Cooper Medical College, he and his assistant have been interested in studying the relation between albuminuria and nephritis and his assistant, Dr. Wm. Osmers, has carried on a long series of investigations of the urines as a routine measure in autopsies. With the findings in the urine and the actual microscopic condition of the kidneys noted, they were compared. The investigation brought out very much the same facts as mentioned by Dr. Emerson. Their experience, Dr. Ophüls said, certainly shows that even a large amount of albumin and casts of any kind may be present in the urine and still, besides chronic passive congestion, no lesions can be recognized at autopsy, either with the naked eye or with the microscope. That is to say, in a large number of the cases the urine showed a considerable amount of albumin and casts in large numbers and all varieties, without inflammatory lesions in the kidney to account for them. This plainly shows what a difficult matter it is to distinguish between the last stages of heart disease and the last stages of kidney disease from an examination of the urine alone. They also found how difficult it sometimes is to recognize even acute kidney lesions by an examination of the urine. In chronic cases urinary analysis often revealed very little, especially in instances where but one examination was made; so that from the pathologic side it must be emphasized that an examination of the urine alone either once or when done repeatedly is not sufficient to make a proper or conclusive diagnosis of the existing conditions. So far as classifying the various types of the disease is concerned Dr. Ophüls agreed with Dr. Shattuck that physicians must adhere after all to an anatomic classification. As to just what this classification should be he is as yet in doubt. He

is sure, however, that it should be based not so much on the minute histologic details but on the grosser features of the disease. A very good sign of what we may be coming to is shown by the report from the Johns Hopkins Hospital, showing that they are attempting to classify their cases of nephritis according to anatomic lesions; they have returned to the oldest anatomic classification, that we possess distinguishing between the large white kidney and the small red one.

Dr. L. Duncan Bulkley, New York, related his own case. in 1869 he had a very severe attack of acute nephritis. He was attacked suddenly and the urine became as black as coffee, thick and solid. He was sick a number of months and was compelled to give up his hospital work. He went to the country. Since then he has had three or four acute attacks, the most severe being eight or ten years ago, when going through the Yellowstone Park. Then the urine was black as coffee, thick and solid. For a few days he took absolutely nothing but milk and then he went to Vancouver and dieted more or less. The plan of treatment he advocates is the taking of pure warmed milk, perhaps a little diluted, one or two hours before eating. He never takes milk with his meals. From that time to this, i. e., for twenty-five years or more, during six days in the week, he consumes a quart of milk a day and takes a moderately fair diet. One goblet of milk is taken at 12:30 and three goblets after 11:30 at night. The milk should be taken between meals and at the temperature of the body so that it can be absorbed immediately and pass into the lacteals, etc. When Dr. Lambert examined Dr. Bulkley for insurance, he said that he would live fifteen years; that time has expired some time ago. Dr. Bulkley has been refused several times by life insurance companies because of the presence of so much albumin in the urine. He has had several policies granted him, however, because before going for examination he has been careful for a few days or weeks. He believes that it is of immense importance to know just what the kidneys are doing day by day, and week by week. He has a number of patients whose urines are tested day by day. He has the entire quantity of urine passed in the day examined in order that he may know the absolute quantity in ounces that is passed and which enables him to mark out the coefficient of the solid ingredients, a thing which he considers to be of more importance than knowing exactly the exact quantity of albumin. One should know exactly whether or not the patient is passing from the body in twenty-four hours his equivalent of solids.

Dr. G. V. McCaskey, Fort Wayne, Ind., said that he thinks that those who have given the dietetic treatment of chronic nephritis careful attention are almost a unit in regard to

the necessity of properly feeding these patients. Several years ago he became especially impressed with the fact that they were underfed. Patients went to him emaciated and weak from the long continued use of toast and slop diets. He then began cautiously to experiment with more substantial diets, gradually introducing liberal quantities of meat. The effects on albumin excretion, casts and the general symptomatology of the case was carefully observed, and these patients were found not only not to do worse, but to do better in every respect. It is not the color of the meat which is the proper criterion, but its digestibility. No general rules can be laid down with regard to the absolute quantity of meat to be given, but he has been in the habit of making a sort of test by giving such a patient a full meal of meat; and if the urea output goes up sharply, it proves to his satisfaction the existence of such a degree of renal capacity as will justify such a diet. He referred to the importance of paying especial attention to the gastrointestinal tract. He thinks it is not saying too much to affirm that in a large proportion of the cases of chronic nephritis, the disease is caused by toxins absorbed from the gastrointestinal tract. The therapeutic importance of this fact is obvious. In many cases the stomach and intestines should be carefully investigated by chemical and microscopic methods, and in many the patient will be greatly benefited by suitable local treatment of the morbid conditions thus revealed. With regard to Dr. Brown's paper Dr. McCaskey does not feel convinced from the data he presents that the kidneys are not at fault in the causation of eclamptic seizures. Of course, there are many other factors, but the increased toxicity of the blood is best explained by inadequate renal function, assuming, of course, the increased formation of toxins. This does not necessarily mean organic renal disease, for the real trouble may be cardiac or vasomotor. Dr. Emerson said that in the degenerative lesions of chronic renal disease the albumin persists longer than the casts. His conclusions are based on an extensive series of cases in hospital practice. Now, if they are to be accepted, it seems to Dr. McCaskey that a logical inference is that albuminuria is a more important indication of degenerative renal disease than the presence of casts.

Of the tests for albumin, he prefers the use of the Janret reagent as the initial routine test in all cases. The formula for this is: Hydrarg. bichlor., 1.35 gms.; potassium iodid., 3.32 gms.; acid acetic, 20.00 c.c.; aquæ, 64.00 c.c. All forms of proteids respond to this test, and can be excluded at once if a negative result is obtained. If the result is positive, then other tests such as those described by Dr. Stengel can be used to determine its clinical significance. Dr. McCaskey referred to the statement in the abstract of Dr. Councilman's

paper, printed in the program: "Interstitial changes in the kidney are secondary to injury of the parenchyma." He said that this statement should not pass without comment, because it tends to convey an impression which the author certainly does not intend, that interstitial nephritis is usually the result of the parenchymatous form which is not in accordance with the facts.

DR. WOODS HUTCHINSON, Portland, Ore., said that the thing we most need to-day is to get a clear conception of the fact that Bright's disease is not primarily a disease of the kidney; its causes exist outside of that organ. In many cases the kidney trouble is the localized result of a general arteriosclerosis or fibrosis, and this is usually due to the presence of toxins in the blood. We can more and more trace this as a cause of nephritis and we are less and less overlooking influenzas, summer diarrheas, ptomain-poisonings, etc., as causes. Whenever there is this toxic condition the kidneys suffer chiefly from their attempt to eliminate. He believes that the importance of albumin and casts has been greatly exaggerated. Really the amount of albumin found in the urine is an unimportant consideration. It is never a symptom of inflammation and the important question is, what is the cause of this intoxication? He believes that food has very little to do with its production and yet we have taken milk as the food in Bright's disease. Milk is an admirable food, blameless and innocent, both in the color and in its association with childhood days, yet he believes it is dangerous in nephritis because of the heavy percentage of work that is thrown on the kidneys, as von Noorden has shown, in proportion to its nutritive content, more so than by any other food. It also swarms with bacteria. In milk shakes, and milk punches the real danger is often from the milk rather than from the alcohol. Although red meat has both the color and attractiveness of sin, yet its actual nutritive value is probably more than that of any other food in proportion to the work it throws on the kidneys. With regard to any diet this must be remembered. The kidneys are there for their own benefit, as well as for ours. What we call excretion or elimination they call feeding. A nitrogenous diet is necessary for the proper nutrition of the kidney cells, and we lower their vitality, as well as that of the body generally, when we cut it off or reduce too low. Any diet that diminishes the amount of fermentation in the intestines of the patient and builds up his strength is the diet that is best fitted in cases of nephritis, regardless of whether it be proteids or carbohydrates, alcohol or milk.

DR. A. P. FRANCINE, Philadelphia, referred briefly to work being done by Dr. Joseph Walsh of the Phipps Institute of Philadelphia, in reference to nephritis occurring in those dying of pulmonary tuberculosis. In all 53 cases have been ex-

amined, both macroscopically and microscopically. The kidneys were sectioned as usual, described and then further cut up. Anything abnormal found was blocked and studied microscopically. From twelve to one hundred microscopic specimens were studied in every case. Frequent and accurate examinations of the urine were also carried on from the time the patients entered the wards. Often the urine analysis was negative, while the kidneys showed a pathologic nephritis. The findings are mainly pathologic. He referred to the more important facts. The following is a tabulated list of results: Normal, 1; congestion, no tubercles, 3; cloudy swelling, scattered tubercles, 1; toxic nephritis, no tubercles, 4; toxic nephritis, scattered tubercles, 10; parenchymatous nephritis, no tubercles, 7; parenchymatous nephritis, scattered tubercles, 8; interstitial nephritis, no tubercles, 1; interstitial nephritis, scattered tubercles, 4; diffuse nephritis, no tubercles, 2; diffuse nephritis, scattered tubercles, 6; cloudy swelling, scattered tubercles, amyloid degeneration, 1; parenchymatous nephritis, scattered tubercles, amyloid degeneration, 1; ulcerative tuberculosis of kidneys (surgical kidneys), 2; scattered tubercles, 1. Thus 34 of the cases show typical tubercles. From the above results of careful examination it may be seen that nephritis in tuberculosis is common. This occurs usually in the form of parenchymatous or toxic nephritis, though other forms are not infrequent. Normal kidneys in connection with tuberculosis are rare. Glomerulo-nephritis or hemorrhagic nephritis was never found. Tubercles were diagnosed as such, only when they showed caseation and giant cells. Thus of the above series 64 per cent., or nearly two-thirds of the cases, showed miliary tubercles. This is a new and important discovery.

Dr. James J. Walsh, New York, said that physicians succeed in doing something for their patients just in proportion to their early recognition of disease and the use of curative and prophylactic measures, to prevent its further progress. The reason why in recent years the death rate from tuberculosis has been so greatly reduced, is that physicians have learned to recognize the very earliest stages of the disease. Many of the patients who are now sent to sanitaria, a few years ago would have been pronounced by most physicians to have nothing serious the matter with them, so slight are the signs of tuberculosis. Indeed, at the present time, the cry of the specialist in tuberculosis is that more patients are not saved, because the family practitioner has not learned to value at their full significance the earliest signs of the affection. The same thing is true with regard to most of the diseases which the medical man has learned to turn over in recent years to the surgeon. It is because appendicitis can be recognized before it produces general peritonitis, and because gallstones and ulcers of the stomach are consid-

ered as worthy of early surgery, that the death rate from these diseases is reduced. If nephritis which has come in recent times to occupy something of the place that tuberculosis held a generation ago, could be recognized during its early stages, then undoubtedly the cure, or at least the prolongation of life with this disease, could be secured as it is in tuberculosis. The kidney symptoms of nephritis are by no means the first to manifest themselves. The urinary symptoms are only manifestations of a local change in the kidney, which has been evident, however, by symptoms from other parts of the body for some time before. It is these early symptoms of constitutional affection, that will eventually lead to the severer forms of nephritis that physicians must try to recognize. There are undoubtedly some clinical symptoms of these earlier manifestations. When the toxins that are eventually to work serious damage on the kidneys are originally absorbed from the digestive tract, they produce only a high tension pulse and a tendency to the disturbance of the heart action. This high tension pulse can be observed in the arteries, and the subjective symptoms of it a fluttering heart with a tendency to the heart beats making themselves felt during a good portion of the day, and especially during severe exertion, not infrequently bring patients to physicians before there are any urinary manifestations or at a time when the symptoms in the urine are so slight as scarcely to attract attention. There seems to be no doubt that much of the nephritis that is seen is due to the fermentative disturbances in the intestinal tract, which disturb digestive processes. Constipation has become such a common ailment in modern times that a medical wag said not long ago that perhaps it is leading and light that our people need, but it seems more probable that laxative and licorice powder are about what they want. As the result of these intestinal disturbances, a certain amount of toxemia is not at all unusual and whenever there are symptoms that seem to point to disturbance of arterial tension and of heart action, in connection with it, the question of prophylactic treatment so as to prevent the development of nephritis should always be considered. Here is where the only hope in the medical treatment of Bright's disease seems to lie.

Dr. Frank Billings, Chicago, said that our conception of nephritis may be compared with affections of other end organs of the body, especially the eye and brain. We know that the eye may be affected by local conditions or because of some general bodily defect; thus vision may be disturbed through local disease of the eye, which does not depend on any systemic condition. Vision may be disturbed through local conditions of the eye which are due to some systemic condition, and again vision may be disturbed without a dis-

ease of the eye, but because of some systemic diseases, a brain condition. If one should attempt to treat the loss of vision without a diagnosis of the causes of the disturbance, it would be irrational. So of the kidney, another end organ may be diseased locally by inflammation or degenerative changes which are manifested by albumin and casts in the urine, without any systemic disturbances. The seriousness of the condition would then depend on the degree of kidney disease. The kidney may be involved in a systemic disease as a secondary process or as a part of the general disease. The kidney may be much or little affected, the seriousness of the condition often depends on the cardiovascular status. A general disease may exist with cardiovascular changes in which the kidney may be little or not at all involved, as is evidenced by a urine that is practically free from albumin and casts and yet the individual may be as thoroughly a subject of Bright's disease as if the urine contained albumin and casts. It is the failure to recognize the diseased conditions of other organs of the body when there may be evidences of disease of the kidney, as evinced by the presence of albumin and casts, that has resulted in an uncertainty as to the management of kidney disease. Drugs may be indicated in certain of these conditions and the food indicated may be entirely different in each of the conditions named above. He said that physicians generally must agree with Dr. Shattuck in his ideas of diet in Bright's disease.

Dr. John H. Musser, Philadelphia, emphasized especially what had been said regarding the classification of nephritis, and the forms of Bright's disease. He also called attention to the importance of making a complete chemical analysis of the urine, a physiologic study, in order to lay down proper lines of dietetic management, as a study of the nitrogen output, and a study of the elements found that are secondary to putrefactive changes in the intestinal tract. The important statements made by Dr. Emerson, he said, should give rise to much reflection, and especially the statement regarding "showers." In one or two instances after the use of salt solution, in cases of interstitial nephritis, Dr. Musser had an opportunity of seeing these extraordinary showers occur. Physicians should not make a final diagnosis in obscure cases of alleged Bright's disease unless the patients are in bed a certain length of time, and the urine examined under such conditions, as well as after exercise and perhaps after various modifications of diet. Finally, he questioned the conclusions that have been drawn from an examination of the urine taken after death. At this agonal period changes occur in all secretions, even though there is no pathologic basis for them.

Dr. M. H. Fussell, Philadelphia, sounded a note of warning. He said that it is unquestionably true that the pres-

ence of albumin and casts in cases of arteriosclerosis is simply a part of the general arteriosclerosis, and it is perfectly right that it should be so recognized. It is equally true that albumin and casts in large quantities may occur in many conditions without there being a true nephritis. If it is shown that albumin and casts occurring in the urine does not mean a nephritis, he is afraid that many general practitioners of medicine will say, "Why examine the urine at all?" It is of the greatest importance that albumin be looked for in a routine manner in much the same way as the heart, lungs and arteries are examined in every case. The presence of albumin and casts does not mean necessarily the presence of a nephritis, but they are danger signals, and if we do not examine the urine carefully, we will not be aware of their presence.

Dr. L. Leroy, Nashville, said that while there is a possibility of giving too much attention, or of placing too much confidence in, urinary examinations, still the present tendency to disparage their value is not in keeping with the highest and best work, and the general practitioner is liable to go to extremes and to disregard these findings. Dr. Leroy believes that it is rather a step backward and not a step forward. The finding of albumin and casts does not necessarily mean that the kidneys are not diseased, nor does it mean that they are. He thinks that the future classification of nephritis will be, as Dr. Billings has suggested, not on the microscopic findings, not so much on the gross anatomic appearances, as on the etiology. Arriving at a prognosis in the presence of relatively small amounts of albumin and casts is one of the most difficult things and this may be a possible explanation of the work Dr. Leroy has been doing during the past two years in examining portions of the kidneys. Frequently he has found a large percentage of the kidney in good condition, whereas certain of the pyramids were in an advanced stage of degeneration. Yet there was sufficient kidney not involved to carry on the work fairly well. With regard to the treatment by diet he has found that the use of boiled meats gives the best results. Boiled meat approximately has as much nutritive value as the unboiled and the process of boiling gets rid of the extractives which are more irritating than useful.

Dr. J. A. Lichty, Pittsburg, Pa., said that it seems to him that we are coming to the turning of the way. We must look in a different direction for the basis of a diagnosis. Physicians should hold to what they have already gained during the past years and add to that some information which might come by a study of blood pressure. He is surprised that the study of blood pressure has not been taken up in this discussion. The sphygmomanometer will yield information in many cases in which the examination of the urine appears to be misleading. He mentioned two cases which he saw re-

cently. One patient was a man 60 years old, who was thrown from a street car and sustained considerable shock, and did not recover as rapidly as Dr. Lichty thought he should. The urine appeared normal. On taking the blood pressure it was 210 and that aroused suspicions that there was more than the results of the accident to contend with. About the same time a pregnant woman consulted Dr. Lichty. Her urine contained casts and an abundance of albumin. The man had a high blood pressure, but no albumin or casts, and he grew gradually worse, and thirty or thirty-five days later he had convulsions and died. Here was an instance of a man having a nephritis and yet no albumin or casts. The woman had a blood pressure of only 110, with an abundance of albumin and casts, and went through her confinement without any suspicious symptoms; after her labor the urine was perfectly clear and she was perfectly well. These two cases show very definitely the value of the sphygmomanometer in the diagnosis of nephritis or Bright's disease. The direction of study now, Dr. Lichty believes, should be more toward blood pressure and probably the infections.

Dr. Alfred Stengel, Philadelphia, declared that the matter of classification of nephritis has been discussed time and again, and it is apparent that no classification can be offered which will prove satisfactory from all points of view. Such working classifications as may satisfy the clinician are inadequate in a pathologic sense. He has considered only acute and chronic nephritis (parenchymatous) and amyloid disease of the kidney, and has set apart chronic interstitial nephritis as a different sort of process. It is very important that physicians should distinguish parenchymatous disease of the kidney or ordinary Bright's disease, whether acute or chronic, from chronic interstitial nephritis. In parenchymatous Bright's disease there is a disorder of renal function which shows itself in disturbed general metabolism and disordered nutrition of varied type. For a long time at least the condition is essentially a renal affair. On the other hand, chronic interstitial nephritis usually is only secondarily and even in a terminal sense a renal condition; primarily, it is a more or less subsidiary part of the general condition, arteriosclerosis. Dr. Councilman and others have established the frequency of acute interstitial nephritis in certain infections, and reasoning from analogy one may assume that chronic interstitial nephritis might result from such a condition without the necessary existence of general arteriosclerosis. As a matter of record, however, Dr. Stengel has seen very few instances of chronic interstitial nephritis without antecedent arteriosclerosis. According to his view, chronic interstitial nephritis is for practical purposes simply a renal phase of generalized arteriosclerosis, just as in other cases one may meet with a cerebral type. It is important to recognize this because the un-

toward results of renal inadequacy are far distant and unlikely events in chronic interstitial nephritis as compared with the parenchymatous forms, and for this reason a differentiation must be made. He said that he thinks that Dr. McCaskey misunderstood Dr. Councilman's meaning in the abstract where he states that "interstitial change in the kidney is secondary to injury of the parenchyma." It is a dogma in pathology that all fibroid or interstitial processes have antecedent changes or degenerations in the parenchyma of the organ. There must be cellular destruction before the interstitial processes arise. Dr. Councilman's thought was this, Dr. Stengel takes it, and not what he presumes Dr. McCaskey believes that all cases of chronic interstitial nephritis are secondary to what we recognize as chronic parenchymatous nephritis. The statement was to be interpreted in an anatomic and histologic sense rather than in this clinical way. Referring to the danger of entire frankness in the matter of pointing out the significance of albumin or of casts in the urine, he agreed that it would be deplorable if practitioners ceased to make routine examinations of the urine, because we here freely acknowledge the deceptiveness of such examinations in certain cases. So far as his own contribution to the subject is concerned he said that there is no difficulty in recognizing established nephritis when one makes repeated examinations of the urine. It is difficult, however, in cases of trivial albuminuria to assert positively whether there is a beginning Bright's disease or some transient condition. Also, it is difficult to assert with positiveness the pathologic significance of albumin and casts in the last days of life, especially when death is brought on by cardiac disease. Repeated examinations are necessary and a study of the case for a considerable period of time enables the physician to reach definite conclusions in all renal cases. Only the routine examination of the urine will lead to a proper understanding of such cases; without it the physician falls into superficial methods of diagnosis.

Dr. Philip King Brown, San Francisco, said that there is no evidence at all to show that there is any intoxication due to the retention of normal end products except in cases of jaundice. He thinks that all investigators have shown that no end products, or intermediary products, have anything to do with the intoxication of eclampsia. None of these products has been found to be uniformly increased in the blood of eclamptic patients, nor has experimental injection of an excess of these products reproduced clinicaly or pathologically the condition of eclampsia. He said that he wished to correct the impression which Dr. McCaskey has, that the cases cited in which the urea was so strikingly diminished, were cases of eclampsia. They were cases of pathologic conditions of the kidneys or cases in which eclampsia had been present before, but the pregnancies during which observations were made were normal.

RECENT ADVANCES IN THE PHYSIOLOGY OF HUMAN NUTRITION.

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The question of the physiology of nutrition is a most important one. It is especially important to the physician, for without a clear idea of the subject he can not prescribe a proper dietary for the well or sick nor can he clearly understand the pathologic conditions which occur as a result of an improper amount or kind of food or the morbid conditions which result from malnutrition.

It is the belief of the layman and of many physicians, too, that the chief nutrition of food consists of the proteids, and meat is especially looked on as the food which affords strength and sustained effort. Among Europeans and Americans especially meat eating is very prevalent, chiefly for the reasons given above. Besides this, the palate is pleasantly excited by rich animal foods, and in consequence a larger amount is taken. It is too common a belief that the well-nourished body is the most healthy and best able to resist disease and that a large fat deposit in the tissue is an evidence of good general nutrition.

Our food is made up of proteids, fats and carbohydrates. The proteid or albumin, both animal and vegetable, is the tissue builder. Relatively, a larger amount of proteid is required for the growing individual, pound for pound, than for the adult. The fats and carbohydrates (sugars and starches) comprise the fuel of the

body and supply the necessary heat and keep the machinery going.

STANDARDS OF DIET.

As a result of the years of experiment by physiologists and of observation by many workers, certain general conclusions have been arrived at in reference to the requisite amount of food which is necessary to maintain health and strength and at the same time afford the best degree of efficiency with the least expenditure of energy on the part of the body to utilize the food. The standards of diet which have been brought forward by different workers do not differ very materially in the amount of the different elements advised for a twenty-four-hour dietary. The standard of Carl Voit of Munich is the one best known and has been recognized chiefly because of Voit's reputation as a successful student of nutrition.

Voit considers that a normal man of an average body weight of 70 to 75 kilos (150 to 165 pounds), doing a moderate amount of work, requires daily 118 gm. of proteid, 55 gm. of fat and 500 gm. of carbohydrate. This gives a total food value of about 3,000 calories and will maintain the body in a good physical condition. The standard introduced by Atwater gives 152 gm. proteid, 125 gm. fats and 400 gm. carbohydrates, affording a fuel value of 3,315 calories.

These standards are based on the idea that from 100 to 118 gm. of proteid or albuminous food is necessary to maintain the body in nitrogenous equilibrium; that is, that the amount of nitrogen excreted through the urine and feces should equal that taken into the body and at the same time the body be maintained in a state of equilibrium as to health, strength and practically also of weight.

Right here it is best to relate the fate of the elements taken into the body. Fats and carbohydrates when oxidized in the body are ultimately burned to simple gaseous products, that is, carbonic acid and water. Consequently the waste from these food products is quickly

thrown out of the body without resulting harm to any of the tissues.

If such products are taken in excess, the harm which results will be chiefly in the deposits of fats in an undesirable amount, which would render the body gross and unwieldy. A too large amount taken is very apt to clog the alimentary canal, overfatigue the digestive organs and may undergo abnormal fermentation.

The waste products of proteid foods, when assimilated, consist of crystalline nitrogenous products which ultimately pass out of the body, chiefly through the kidneys. Before their elimination from the body these crystalline elements, which are in some instances toxins, float about through the body and may exercise a deleterious influence on the organism either general or local. The literature is full of theories on the diseases due to many of these crystalline products, chiefly uric acid, urea, the purin bodies, etc. All who are acquainted with these facts have recognized the importance of restricting the formation of the deleterious crystalline waste products by limiting as far as possible the amount of proteids taken into the body.

Until recently it has been the belief that the nitrogenous equilibrium of the body could not be maintained on a less amount of proteids than that given in the standard diet of Voit and others.

Recently some far-reaching experiments have been made on the physiology of nutrition and of metabolism of the body which practically revolutionize the ideas held by most physiologists, and it is the chief purpose of this paper to call attention to these new facts.

They are chiefly contained in an experimental study by Russel H. Chittenden, director of the Sheffield Scientific School of Yale University and professor of physiologic chemistry, on the "Physiologic Economy in Nutrition, with Especial Reference to the Minimum Proteid Requirement of a Healthy Man," and two articles by Otto Folin on studies made in the chemical laboratories

of the McLean Hospital for the Insane, Waverly, Mass., on "Laws Governing the Chemical Composition of the Urine" and "A Theory of Protein Metabolism."[1] Bearing on the same subject to a lesser degree is the classical work of Prof. J. P. Pawlow of St. Petersburg, on "The Work of the Digestive Glands."

In the foregoing and in what follows I have made free use of the data found in the above-named books and periodicals and without further acknowledgement of my indebtedness to these eminent writers, I desire above everything else to recommend these books for a careful study by all who are interested in this subject. If this article accomplishes nothing more than to induce this audience to study the works named, I feel that it shall have accomplished a great deal.

With the object of throwing light on the subject of the physiologic economy in nutrition, Professor Chittenden made experiments on three groups of men.

The first comprised a group of five men, of varying ages, connected with the faculty of Yale University, whose work was distinctly mental rather than physical.

Second, a detail of 13 men volunteers from the Hospital Corps of the United States Army, as representatives of the moderate worker. These men were of different nationalities, ages and temperaments.

Third, a group of 8 young men, students in Yale University, all of them trained athletes, as combining the mental worker with a pronounced amount of physical work.

The individuals of these groups were experimented on by permitting them to have first the usual standard dietary, during which urinary examinations were made showing the nitrogen output together with the weight, strength, and physical and mental efficiency of the individual. Then for a long period of months each individual of each group was placed on a dietary which

1. Amer. Jour. of Physiology, vol. xiii, Nos. 1 and 2.

diminished his proteid food to one-half or less even of the Voit standard but permitting the individual freedom in his choice of fats and carbohydrates to the full satisfaction of his appetite. On this dietary the body weight diminished to a very moderate degree in some of the individuals, but soon became constant and the health, strength and efficiency, both mental and physical, was maintained at a higher level than on an ordinary standard diet. On the Voit diet or its equivalent the daily excretion of nitrogen through the urine amounted to at least 16 gm. On the diet with a much lessened amount of proteids the daily output of nitrogen amounted to about 6 to 9 gm. The nitrogenous balance was maintained on this diet, as shown by a practically constant body weight in each individual, especially after the individual had been on the diet for a few days, and by an estimation of the nitrogen output in the urine and feces. The diminution in the nitrogenous waste materials was chiefly in the urea nitrogen. The total output of uric acid in the urine was also diminished. Professor Chittenden did not take an account of the excretion of the kreatinin or of the sulphur compounds, but Folin made such observations, which will be quoted later. Chittenden showed undeniably that the men experimented on, who represented all classes of individuals in reference to mental and physical work, could meet all ordinary requirements of mental and physical labor with a high efficiency on an intake of proteid food far below that of the standard diets. It was found, too, that in the reduction of the proteid it was not necessary for these individuals to increase very much, if at all, the amount of fats and carbohydrates to maintain themselves in good condition.

Professor Chittenden comments favorably on the practice of a more thorough mastication, as brought out by Mr. Horace Fletcher "In the A B Z of Our Nutrition" and of the existence of a reflex of deglutition evoked by thorough chewing, which, if properly carried

out, produced a very striking effect on the appetite, which was made more discriminating and led to a choice of a very simple dietary and in part reduced the craving for flesh food.

Those who have found it necessary to lavage the stomach of patients have noticed the very common want of a thorough division of the food by mastication, as shown in the large particles of food of all kinds which are found in the stomach of the average individual. This entails an enormously increased work on the digestive organs and one of the salutary lessons of the stomach tube to the patient is to show him the evils of insufficient mastication. That mastication should be carried out to the degree and for the purpose advised by Mr. Fletcher and Dr. van Someren is a question which time must solve. We are too apt to be faddists in many ways, but if the gentlemen named shall influence the observance of the physiologic law of thorough mastication of the food they will have accomplished much good.

Otto Folin, in the analysis of the urine from many individuals on a standard diet, found that the total nitrogen excreted in twenty-four hours averaged, in round numbers, about 14½ to 18 gm. This amount of nitrogen was represented by urea in from 86 to 90 per cent.; ammonia in from 3.3 to 4.5 per cent.; kreatinin in from 3.2 to 4.5 per cent.; uric acid in from 0.6 to 1 per cent. and undetermined nitrogen in from 2.5 to 5 per cent. On a dietary with a minimum amount of proteid, far below that of the standard diets, but still sufficient to maintain nitrogenous equilibrium and practically a constant body weight, the average nitrogen output in the urine diminished to 4 to 8 gm. in twenty-four hours. The percentage of urea nitrogen was now diminished to about 60 per cent.; the ammonia nitrogen was totally diminished, but the percentage was relatively slightly increased. Kreatinin remained the same in absolute quantity excreted. Uric acid was diminished in

total amount, but not nearly in proportion to the diminution of the total nitrogen, and the per cent. of uric acid was therefore relatively increased.

In normal individuals, on a standard diet, the total sulphur output was 3 to 3.75 gm. in twenty-four hours. This was made up of inorganic SO_3—ethereal SO_3 and neutral SO_3. Of these, the inorganic SO_3 made up an average of 87 to 89 per cent., the ethereal 5.5 to 8 per cent., and the neutral 4 to 6 per cent. On a low protein diet the total sulphur excreted ranged from 0.77 to 1.50 gm. in twenty-four hours. This was represented by inorganic SO_3, reduced to about 60 per cent. The ethereal increased to about 14 per cent., representing a form of sulphur metabolism more prominent with than without the protein. The neutral sulphur was relatively increased, but the total excretion was the same—that is, unaltered in amount by the reduction in the proteids.

That the above statements may be made more graphic, I copy from Folin's article[2] the following, showing the analysis of the urine from the same individual, taking a standard diet in the first, and when taking the diet, with a much reduced protein in the second column.

	I.	II.
Volume of urine	1170 c.c.	385 c.c.
Total nitrogen	16.8 gm.	3.60 gm.
Urea nitrogen	14.70 gm. = 87.5 p. c.	2.20 gm. = 61.7 p. c.
Ammonia nitrogen ..	0.49 gm. = 39 p. c.	.42 gm. = 11.3 p. c.
Uric acid nitrogen...	0.18 gm. = 1.1 p. c.	0.09 gm. = 2.5 p. c.
Kreatinin nitrogen ..	0.58 gm. = 3.6 p. c.	0.60 gm. = 17.2 p. c.
Undetermined nitrogen.	0.85 gm. = 4.9 p. c.	0.27 gm. = 7.3 p. c.
Total SO_3	3.54 gm.	0.76 gm.
Inorganic SO_3	3.27 gm. = 90.0 p. c.	0.46 gm. = 60.5 p. c.
Ethereal SO_3.....	0.19 gm. = 5.2 p. c.	0.10 gm. = 13.2 p. c.
Neutral SO_3	0.18 gm. = 4.8 p. c.	0.20 gm. = 26.3 p. c.

A glance at the table shows clearly the relation of the different forms of N and SO_3 excreted by the same individual on the two diets.

It is shown that the total N excreted is diminished from 16.8 to 3.60 gm.; that urea N is greatly diminished from 14.7 to 2.2 gm.; that ammonia N is but moder-

2. Amer. Jour. of Physiol., vol. viii, No. 2, p. 118.

ately diminished from 0.49 to 0.42 gm.; that uric acid N is diminished one-half, from 0.18 to 0.09 gm., and that kreatinin N is practically unchanged in the total amount excreted. It follows that the percentage relation of the different N bodies is relatively altered—with the marked diminution alone of the urea N.

With the SO_3 output, inorganic SO_3 corresponds in fluctuation in the two diets with urea, ethereal SO_3 with uric acid, and neutral SO_3 with kreatinin.

If one will compare the table of analyses of urine in the reports of Chittenden and Folin they will be found to correspond in the main in reference to the N output. Chittenden's observations were made on individuals over a sufficiently long period of time to show that the result is definite, and Folin's more complete estimation of the different forms in which N is excreted and the relation of one to another affords us data on which a fundamental theory of metabolism may be considered.

There are at present two theories of protein metabolism. According to Voit, protein of the food circulates in the blood and plasma of the tissues, and is there katabolized without becoming an integral part of the cells. Essentially this constitutes chemical decomposition of the protein in solution. The small part of the living cells which dies is dissolved in the circulating medium and becomes a part of the protein derived from the food.

Pflüger's theory is that the circulating protein of the food is first transformed into bioplasm, becomes a part of the living cell and as such is oxidized. Pflüger admits that a part of the protein may be katabolized in solution according to the theory of Voit.

The theory of Pflüger involves an enormous building up of bioplasm, coincident with an equal destruction of tissue. Both theories involve the katabolism of all of the protein of the food, in the tissues where they are utilized.

As Folin says, no fundamental theory concerning pro-

tein metabolism can be accepted unless it can be made to harmonize with the laws governing the composition of the urine.

The theories of Voit and Pflüger are based on the assumption that quantitative changes in the total protein metabolism produce no appreciable effect on the percentage composition of urines, representing such metabolism. As announced by Folin, changes in the total amount of N and S eliminated in the urine show a pronounced change in the percentage composition of the N and S.

This seems to prove that katabolism of protein food must be of at least two kinds. The nature of the changes in the distribution of the urinary constituents seems to warrant the statement that the two forms of katabolism are independent. The one is variable in quantity, as represented by urea and inorganic sulphur, the other is constant and yields kreatinin, neutral sulphur and to some degree uric acid and ethereal sulphates.

As is shown in the urine analyses, the more the protein of food is diminished, and therefore katabolism reduced, the more prominent relatively become kreatinin and neutral sulphur the representatives of the constant katabolism.

It has been proved that kreatinin elimination is not diminished, and that some other constituents are but slightly reduced when practically no protein food is given. This shows that there is a constant tissue waste, varying possibly in degree with the wear and tear incident to work, and shows that a certain amount of protein must be furnished with the food to maintain nitrogenous equilibrium.

In other words, katabolic processes which yield the end products that are a constant quantity under varying amounts of proteid food, represent the metabolic processes that constitute an essential part of the activity which distinguishes living from dead cells.

Folin distinguishes the constant protein metabolism,

a tissue or endogenous, and the variable protein as an exogenous or intermediate metabolism. The constant metabolism fixes a limit to the lowest attainable level of nitrogenous equilibrium. Just what this level is will depend on how much, if any, urea is derived from the same katabolism which produces kreatinin. When this shall have been determined we shall possess a formula, expressing the point of lowest attainable protein katabolism, because at this point the percentage composition of the nitrogen and sulphur of the urine will be constant. It is plain that a sufficient amount of protein food to maintain the constant protein metabolism will be absolutely necessary.

The existing theories assume that protein metabolism is essentially an oxidation, and that the greatest amount of katabolism takes place in the muscles where the greatest amount of oxidation exists, i. e., the same chemical processes as those which katabolize the fats and carbohydrates.

Folin makes it clear that the splitting of the protein molecule may be more easily accomplished by hydrolysis than by oxidation.

Urea is not found in the muscles except in very small traces. Its absence in the muscles where the greatest katabolism takes place has heretofore not been explained. On the other hand, kreatin is found in the muscles, and its derivative kreatinin is a constant quantity in the urine.

If the katabolism of proteids represented by urea does not take place in the muscles, then it must be that the nitrogen katabolism which yields urea must take place elsewhere by special chemical processes. Furthermore, we are forced to the conclusion that this katabolism is not of such fundamental importance as that which yields kreatinin. It is known that in the digestion of protein, ammonia is directly formed by proteolytic ferments, and that the liver is capable of converting ammonia into urea. It is known, too, that the blood passing from the

intestines to the liver contains two or three times as much ammonia as the blood in the hepatic veins.

Furthermore, there is evidence that hydrolytic decomposition of protein occurs in the digestive tract. The first step in the process is the decomposition into proteoses, amido acids, ammonia and possibly urea. Hydrolysis is carried further in the mucous membrane of the intestines, and is completed in the liver, each splitting being such as to further the formation of urea.

By this means the unnecessary nitrogen is removed, and it explains the fact that the animal organism tends to maintain a nitrogenous equilibrium within the wide limits of forced feeding, on the one hand, and of low protein food experiments on the other.

An excess of protein in the food is not stored up in the body as such, for the actual need of nitrogen is very small, as it is limited to the actual building up of the cell bioplasm. It is not necessary to store it in the body, because an excess of nitrogen is always furnished with the food. A larger nitrogen intake than is necessary to meet the needs of endogenous metabolism will lead only to an increase in the elimination of urea. It can not increase the tissue metabolism and the resulting formation of kreatinin.

The katabolism of fats and carbohydrates is accomplished chiefly by oxidation. The process sets free a large amount of heat, which may be converted into mechanical energy. In the removal of nitrogen from protein by hydrolysis but little energy is expended. The non-nitrogenous rest of proteid decomposition by hydrolysis affords a substance which may be further partly converted into fats or carbohydrates. It then becomes subject to the same laws governing the katabolism of fats and carbohydrates. The organism may at any time be made to store up fats and carbohydrates, if an excess over the requirements is taken. It has already been stated that this excess may be taken without fear of poisoning the body, because the waste from them con-

sists of non-crystallizable products. An excess may overburden the digestive organs and cause abnormal fermentation or tire out the glycolytic function. Too large a deposit of fat may render the body unwieldy and may infiltrate and physiologically embarrass the muscles and viscera.

NITROGENOUS EQUILIBRIUM.

The above theory of metabolism of Folin explains the persistent tendency of the normal body to maintain nitrogenous equilibrium when a large amount of proteid is consumed, even when this involves the formation of an excessive amount of urea.

If one will examine the tables of the feeding experiments made by Folin and compare the nitrogenous output on the low protein diet with the nitrogen excreted in the urine on a resumption of a free amount of protein in the food, it will be seen that the elimination of nitrogen was more than doubled on the first, and on the second day there was more than three times as much excreted as on the last day of the low protein diet.

Folin offers the following explanation:

All the living protoplasm in the animal organism is suspended in a fluid, very rich in protein, and on account of the habitual use of more nitrogenous food than the tissues can use as a protein, the organism is in possession of approximately the maximum amount of reserved protein in solution that it can advantageously retain. When the supply of food protein is stopped, the excess of reserve protein inside the organism is still sufficient to cause a rather large destruction of protein during the first day or two of protein starvation, and after that the protein katabolism is very small, provided sufficient non-nitrogenous food is available. But even then, and for many days thereafter, the protoplasm of the tissues has still an abundant supply of dissolved protein, and the normal activity of the muscles is not impaired. When 30 or 40 gm. of nitrogen have been lost by an average-sized man during a week or more of abstinence from nitrogenous food the living muscle tissues are still well supplied with all the protein they can use. This is proved by the unchanged kreatinin elimination and by the fact that the individual feels no unusual fatigue or inability to do the customary work. The organism at the end of a low protein diet experiment still has an abundance of available protein in the nutritive

fluids, and this is why it only gradually and only under the pressure of an excessive supply of food protein again acquires the original maximum store of this reserve material.

Based on the above interpretation of metabolism and nitrogenous equilibrium, the so-called standard diets are unnecessarily rich in proteids. It is necessary to supply protein in the food in sufficient amount to provide liberally for the endogenous or tissue metabolism and to maintain a reserve protein in solution. If the blood is in need of tissue builders, the organism can rapidly assimilate large amounts of nitrogenous food. This is clearly shown in emaciated conditions following fevers, surgical operations, etc., for during convalescence there is often a ravenous appetite and a rapid increase in weight and strength with a corresponding retention of nitrogen.

The main contention of Voit and others is that it is necessary to consume 118 gm. of proteid daily in order to maintain a nitrogenous equilibrium and at the same time preserve a condition of health and mental and physical efficiency.

The experiments of Chittenden are so decisive that a proteid rich diet is proved not to be necessary. He is unquestionably right in the conclusion that the standard diet may be divided by two, as far at least, as the proteids are concerned.

The practical results of the experiments of Chittenden are made more rational and clear by the researches and deductions of Folin.

THE DAILY DIET.

Chittenden maintains that the daily requirement is not only much less of protein than that recognized in the standard diets, but that the fats and carbohydrates also may be considerably diminished.

We recognize the fact that the diet must differ for individuals, dependent on the occupation, the season of the year, the climate, etc. However, the modification in the diet will consist chiefly in the variation of the

amount of fats and carbohydrates rather than a change in the quantity of the proteid. Folin has shown that physical activity does not cause a material tissue waste of muscle, for kreatinin is not appreciably increased in the urine by physical labor. The growing individual and the emaciated convalescent only can utilize a large nitrogen intake and retain it. The difference in the dietary of grown normal individuals will consist mainly in the fuel foods—the fats and carbohydrates.

The achievements of the Japanese on a diet chiefly carbohydrate is sufficient proof that a high efficiency, both mental and physical, may be maintained on a low proteid and full fuel diet.

If a large proteid diet is unnecessary, is it also detrimental? In the light of the theory of exogenous metabolism of Folin, an excess of proteid furnished with the food is normally rapidly converted into harmless urea and is quickly eliminated by the kidneys.

The excessive production of uric-acid, xanthin bases, kreatin and other so-called extractives is looked on as the cause of gouty and other so-called autointoxication diseases. The excessive production of these substances is usually ascribed to an excess of proteid consumed. These substances are the result chiefly of the endogenous metabolism, and, scientifically speaking, have no relation to an excess of protein, for that substance is converted into harmless urea. However, the meats contain considerable extractives or substances out of which they may be formed, and therefore an excess of concentrated protein food in the form of meat may result in such an autointoxication. The continued excessive use of protein may lead in time to the accumulation of a larger amount of reserve protein than the organism can retain in the fluid media. The continuous presence of such a large unnecessary supply of unorganized reserve material may weaken one or all of the living tissues.

We are the creatures of habit. With palates craving

for new sensations and the prevalent belief that hearty eating promotes health and strength, it is no wonder that we eat too much. It is proper, too, that the pleasures of the palate should be gratified. The pleasure which eating affords promotes digestion. Bolting does not permit proper enjoyment of food. Thorough mastication undoubtedly makes the palate more discriminating and serves as a check to overindulgence.

Chittenden says: "Physiologic economy in nutrition means temperance and not prohibition. It means full freedom of choice in the selection of food. It is not a cereal diet nor vegetarianism."

Practical application of the newer ideas of metabolism and nutrition to diets in disease could be readily made, but are outside of the limits of this paper.

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METHODS, VALUE AND LIMITATIONS OF THE KNOWLEDGE OF THE GASTRIC CONTENTS.

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I think it will be admitted that instrumental and laboratory examinations with reference to the stomach are unduly neglected in practice. The reasons for this are similar to those that cause the neglect of other diagnostic manipulations—technical difficulties, real and imaginary, and erroneous views as to clinical value. Many fail to make examinations of stomach contents solely because they think the passage of the stomach tube is difficult and often objected to by the patient. Contrary to this view, I find very few people who require any persuasion and still fewer who offer serious verbal or physical difficulty. Out of many thousands examined, I have encountered only two people in whom I could not successfully use the stomach tube at the first trial. I am not considering, of course, the very important contraindications to the use of the tube (necessary to remember in every case), or real obstructions to the passage.

A belief in the excessive technical difficulties of the examination of the stomach contents depends chiefly on lack of training and of practical experience in the necessary manipulations, which are not essentially as difficult as some of the methods proposed may indicate. An important cause of neglect comes from disappointment at the results. Those who expect to make complete and satisfactory diagnoses from single features, as Bright's

disease from albuminuria, diabetes from glycosuria, or pneumonia from crepitant râles, discard gastric diagnostic methods when they find out that absence of free HCl does not positively mean cancer. We still find evidences of a belief in the existence of diagnostic signs, in the advocacy of tryptophan reaction, and others, but the probabilities are that in stomach diagnosis, as in other lines, the greatest assistance will come from patient efforts to appreciate the alterations of function and structure primarily, and by allowing our diagnosis to grow out of these findings, assisted by the other clinical features of the case. An appreciation of gastric physiology confirms this *a priori* view. The important rôle of HCl in the stomach contents suggests in the very beginning the usefulness of an examination into the presence, amount and condition of this, whether partly free or only combined or absent. Clinical experience, I think, confirms this, but there are many who fail to realize it. Thus it happened that at an early period, the absence of HCl in cancer of the stomach was noted, and many people grasped at this as a diagnostic feature, and even yet use it as such, although its limitations have long been abundantly demonstrated. On the other hand, some have gone to the opposite extreme, and, discovering the limitations, reject all stomach examinations as useless. Both are wrong. The absence of HCl in cancer is so frequent, and when it does exist, so constant from day to day, as to form a valuable aid, but there may be cancer present with HCl secretion preserved for a long time, even in excess of the normal amount. But such exceptions and contradictions occur in all branches of diagnosis, and should teach us to discover other details, rather than lead us to a condition of despair. I do not think it necessary at this time to give any statistics as to the relative frequency of the presence or absence of HCl in cancer; for, while interesting and valuable, they do not apply to an individual case. In the examination of a patient

we can not give up a diagnosis because of a negative result in one sign. We have still to work out all the signs and only then to attempt the final diagnosis.

In gastric ulcer the excessive secretion of HCl has so often been noted that it is rightly considered one of the signs of the disease, and yet I could cite a number of cases, confirmed by operation, in which there was no excess in repeated examinations. That single or few examinations may be misleading can be shown by some cases in which variations occur, as from 26 to 88 in the course of seven tests extending over ten days. In diseases like cancer and simple ulcer there are such urgent reasons for early diagnosis that all the other diagnostic features should be used as quickly as possible whenever these diseases are suspected, and in these the complete routine examination of the stomach contents will almost always prevent error from exceptional behavior of the HCl.

The value of estimations of HCl, in my opinion, is greatest in functional diseases of the stomach, or perhaps it would be more exact to say cases in which the stomach functions are altered, without gross organic disease primarily in that organ, though there may be functional or organic disease in other organs that may have a part in the production of the gastric anomaly. These conditions are very common, much more so than is often supposed. Excessive secretion of HCl, for example, is a very common condition. While it may be associated with organic changes in the stomach, such as ulcer, spasm of the pylorus, retention, stagnation and dilatation, yet there may be no gastric symptoms, or only trifling ones, for it also occurs with distant symptoms, such as headache (often simulating ocular headache), severe neurasthenia sometimes, in the male, associated with functional impotence, and hence the cause of ill-directed and not rarely harmful treatment. Thorough examinations of the stomach, made as a routine measure, sometimes lead quickly to improvement of

all the subjective symptoms. Even when the gastric symptoms are marked, test meals with complete examinations are indicated. While the picture of marked gastric hypersecretion is often very typical, I have seen cases that had not been differentiated before by other physicians, and that I could not differentiate without test meals, in which the primary conditions were just the opposite—absence of HCl with excessive production of organic acids.

There are also very troublesome cases of functional gastric disease in which the chemical conditions vary. Hypersecretion and hyposecretion or even achylia may alternate in a way only to be followed up by repeated examinations. In the case of organic diseases of the stomach, the further steps are comparatively independent of HCl determinations, but even in these occasional tests are useful. In functional diseases the greatest results often follow frequent estimations of HCl, under various kinds of dietetic and other treatment, and with various test meals. The treatment should be begun as early as possible, sometimes before the first test meal, and used as a factor in the examinations.

There is still room for further investigation in the methods of gastric chemical examinations, and those who have the proper training and facilities can with great advantage pursue such investigation. The general practitioner, however, need not be discouraged because of the possibilities of future discovery, nor prevented from carrying out the methods now available, for these are sufficiently accurate for clinical purposes and not too intricate for any one, and the application of all I shall mention does not require as much time as it does to speak of them. For the primary reaction, litmus paper should be used, and for the presence or absence of free HCl, Congo paper or solution may follow, though this can be dispensed with. Those working with it can learn much from this test. The more accurate and delicate Guenzburg's reagent should always be used.

It is so delicate and exact that I can not understand its frequent neglect. This may be due to erroneous results from using a decomposed solution. The tendency to decompose is a drawback, I admit, but it is so easy to test the solution with a drop of dilute HCl that the fault is a trifling one.

Given free HCl, it is next necessary to determine its amount, and for this the dimethyl-amidoazo-benzol is most satisfactory, though it requires the usual care in practicing with test solutions to get the proper end reaction. For the total acidity the phenolphthalein reaction is used. Tests for the combined HCl are not necessary if there is free HCl, hence all of the steps of Toepfer's method are not required in ordinary clinical work. If there is no free HCl, the qualitative Sjoequist test should be applied. Quantitative estimations for combined HCl are not, in my opinion, of clinical necessity, and in order to be accurate, and hence of value, require more chemical experience than the general practitioner need be expected to have. With proper apparatus and reagents, any one can easily acquire sufficient experience in the estimation of HCl to utilize that substance in diagnosis, and with such experience the quantitative tests can often be omitted. Of abnormal or pathologic acids, lactic is the only one requiring chemical tests, for though acetic acid or butyric acid often occur in large quantities they can be detected by the odor. Lactic acid tests to be most useful should be made on a lactic-free test meal, such as shredded wheat or the Boas gruel. Quantitative methods are not necessary, as the relative intensity of the reaction with Uffelmann's or Kelling's test give sufficient indices, though Strauss' burette may be used. The determination of pepsin is not necessary in ordinary work, since pepsin is rarely absent when HCl is present in sufficient quantities, but the method of Mett is often a useful addition to other tests in obscure functional diseases. It is fairly easy to work, and, with the

valuable details regarding time-limit worked out by my colleague, Dr. Cowie, requires very little time. The existence of the digestive functions and their relative completeness can easily be shown by the biuret and starch tests, and by the changes in the cells of the gastric contents as observed in the microscopic examination. At the same time the experimenter may have his attention called to the advantage of further work with the functional tests proposed by Sahli, some of which promise useful additions to our diagnostic methods.

If I have spoken of chemical tests first it is not because I look on these as all-sufficient, but rather because they are simple and the results are easily expressed in figures or symbols; but without other observations they are of little or no value. The other tests require practical knowledge and experience. Nevertheless they will repay one the time spent in becoming familiar with them either in a clinical laboratory under the supervision of an expert or worked out with the aid of textbooks and clinical material without such supervision. One quickly learns the normal limits regarding the amount, color, consistency and odor of the gastric contents. From these the need of further examinations becomes quickly known. An excess of mucus can also be recognized, and along with this, the fact that it is not always easy to draw a positive conclusion from such an excess. In the first place, it is always important to exclude an origin from the nose, pharynx or bronchi; in the next place it is necessary to be sure that the excess has not been caused by awkward manipulation of the tube, even if unavoidable. But even if we can exclude such factors, it is important to remember that the presence of even considerable mucus does not warrant a diagnosis of chronic gastritis. Blood is easy to recognize when present in large amounts. Small quantities of blood, due to scratching with the end of the tube, are usually easy to recognize. The tests for occult blood developed in the last few years are of con-

siderable clinical value, though it is, of course, necessary to exclude traumatism. The presence of pus is always important, but here, too, we must be able to exclude an origin from the respiratory tract. The appearance of the other cells mixed with the pus, dust pigment and also a greater variety of bacterial forms than occurs in stomach contents, serve to differentiate. The examination of bits of mucosa is not of very great clinical value. In about one-third of the cases in which such specimens have been examined in my clinic, the microscopic examination of the bits coincided with the other findings. But, on the whole, such examinations do not repay the time spent on them, for purposes of practical diagnosis. The examination of the bacteria in the stomach contents is of only limited value. Staining is rarely necessary, though the Wright stain is easy to apply, and stained preparations will be preferred by those who have not had considerable experience with fresh material. Large numbers of bacteria in the stomach contents, however, throw an important light on the question of stagnation, and there are certain variations in the flora in different cases that are of a good deal of aid in diagnosis. So the Oppler-Boas bacillus, and, on the other hand, yeasts and sarcines, often occur in such large numbers as indicate pretty accurately the chemical and anatomic alterations present. Protozoa also have only a limited diagnostic value, but their occurrence in the stomach is interesting, and the study of cases in which they occur may throw a good deal of light on hitherto obscure processes in that organ. The testing of the freezing point of stomach contents or of its surface tension may furnish a useful possibility of work for those who have time, but at present these possibilities are not necessary for clinical work.

In conclusion, my opinion is that examinations of the gastric contents give information that can not be obtained in any other way, and, though often negative, can

not be excluded without risk of serious error. Such examinations are indicated in all stomach syndromes, in all diseases seriously affecting metabolism and nutrition, and in all diseases that affect the function of the stomach, notably diseases of the lungs, heart, liver, kidneys and blood.

CERTAIN NON-GASTRIC DISEASES WITH GASTRIC SYMPTOMS.

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The subject is so vast that a certain amount of abruptness is necessary in the presentation. Some of the minor non-gastric diseases with gastric symptoms may be omitted. The question is a study in etiology. In one sense it may be said the account is to include gastric disorders which are secondary to other diseases. It is not to gastric disorders, but to diseases, remote from the stomach, which have gastric symptoms, that we call attention. Strictly speaking, the gastric symptoms are not due to any organic disease of the stomach; but such division is largely arbitrary. No pronounced gastric symptoms are liable to prevail without either irritation, congestion or inflammation, whether the symptoms are temporary or permanent.

It is understood, then, that the ailments considered are those which have for their chief, and for the time dominant, expression, gastric symptoms; it is the class to which, in loose terms, we say it is not your stomach, but your eyes, or your lungs, or your kidneys that are at fault. The patient's sensations direct him to the stomach alone. We must clearly understand that, although we decide that the gastric symptoms are the minor factors, from the standpoint of therapeutics, we must direct treatment as boldly to their alleviation as to the primary disorder. The eyes may be corrected, but the gastric symptoms only mitigated.

NON-GASTRIC ORGANIC DISEASES PRESENTING GASTRIC SYMPTOMS.

The Eyes.—The subject is familiar to all. Who has not seen correction of errors of refraction relieve so-called "bilious attacks," periodical vomiting, anorexia, indigestion and other gastric symptoms? The cure of grave organic ocular defects relieves similar gastric conditions.

The Ear.—The vomiting of middle-ear disease, of disease of the attic and of auditory-nerve affections is well known.

The Nose and Throat.—Morning nausea, loss of appetite and chronic dyspepsia secondary to the pharyngitis of smokers, occurs to all. The gastric disorders of adenoid disease must also be emphasized.

Nervous System.—I can refer only to the gastric crises of locomotor ataxia; the gastric symptoms of bulbar palsy; the occurrence of vomiting, often for six hours before an attack of apoplexy;[1] the vomiting of meningitis, tubercular and cerebrospinal; the gastric symptoms of brain tumor, and those which precede a fully-developed epilepsy. The call can not be too loud to this latter ailment. Such incidents as periodical attacks of indigestion or of vomiting may precede or attend obscure forms of epilepsy. Patients with the peculiar chewing and rumination in that form of epilepsy to which Spiller has recently called attention are usually treated for stomach disorder. The nocturnal and intermittent character of the attacks, the clinical course and the occasional occurrence of a true attack, with other suggestive symptoms, such as the aura, somnolence and forgetfulness of the event, suggest the true nature of the affection. In children, the occurrence of gastric symptoms, admittedly not of local origin, must demand an examination of the nervous system.

The Cardiovascular System.—The acute affections

1. "Some Clinical Aspects of Vomiting," Univ. Medical Magazine, Nov. 1889. Read before Amer. Med. Assoc., Newport, 1889.

may have epigastric pain and vomiting as sole expressions of the disorder.[2] More pronounced and continuous are the gastric symptoms, often dominating the picture, in failure of compensation. It is not infrequent that dyspnea, palpitation, cardiac pain or dropsy are absent, and yet dilatation of the heart and secondary portal congestion are present and cause gastric symptoms, as pain, vomiting, hemorrhage, loss of appetite, and symptoms of catarrhal gastritis, as the only symptoms of the heart disease. Many patients with dyspepsia and gastritis may be cured with digitalis.

The Lungs.—Apex pneumonia (pneumococcus infection) and tuberculosis are examples; and, in children with severe vomiting, the possibility of the former infection should be borne in mind.

The Liver.—Organic disease and cholelithiasis have their gastric symptoms.

The Intestines and Appendix.—The recent literature is replete with information and common experience leads to an investigation of these structures in acute and chronic gastric disorders.

The Genitourinary Tract.—The gastric manifestations are well known. A renal calculus, an acute or chronic nephritis, may have vomiting, nausea, anorexia or the gastric neuroses as most marked symptoms. Is not uremia often attended by gastric symptoms only?

The Blood.—Iron cures many, many patients with gastric disorders. The perverted appetite and the nausea and vomiting of chlorosis are familiar.

The Infections.—I shall only call attention to the importance of the possible occurrence of gastric symptoms alone in the early periods of the eruptive fevers. Time compels exclusion of uncinariasis, malaria and other infections, and admits of only a word regarding tuberculosis, gonorrhea and syphilis. Tuberculosis

2. "Abdominal Pain," Amer. Med., March, 26, 1904. Read before N. Y. State Med. Assoc., Albany, Jan. 26-28, 1904.

must never be excluded as a possible factor in the production of gastric symptoms. Who has not seen advanced phthisis treated in the early periods of disease for gastric symptoms alone? In young adults, the temperature alone may guide us to a conclusion.[3] The causeless anorexia, the dyspepsia, the morning nausea, and the vomiting may attend early tuberculosis and precede pulmonary symptoms and physical signs. Syphilis is often marked by gastric symptoms, independently of the medication which often causes them. Gonorrhea requires more than a passing notice. In late adult and in early middle age, toxic gastric symptoms occur and continue unrelieved until, if possible, the deep urethral infection or prostatic infection is cured. The history and the urine may disclose the cause.

The Intoxications.—To the toxemia of the infections we must add those due to tobacco and to lead, as in the achylia of plumbic gastritis, as pointed out by Sailer. The objective signs of lead poisoning may be most obscure. Exophthalmic goiter gives rise to pronounced symptoms of gastric character alone, the other phenomena being in abeyance. Protracted vomiting may be of such origin and require careful examination to disclose the source. The presence of pus somewhere will give rise to gastric symptoms, and I have long taught that anorexia is often due to internal suppuration.[4] Addison's disease may cause toxic gastric symptoms while uremia is a classical cause.

NON-GASTRIC CONDITIONS ATTENDED BY GASTRIC SYMPTOMS.

To this division belong that very large class of cases to which the term gastric neurosis is applied. Gastric symptoms may be the only manifestation of hysteria and of neurasthenia. The gastric neuroses are the most

3. "Gastric Symptoms of Tuberculosis." J. H. Musser.
4. "The Gastric Disorders of Pulmonary Tuberculosis," University Medical Magazine, July, 1891.

difficult to understand. Unfortunately time forbids any complete discussion.

ACUTE GASTRIC MANIFESTATIONS SIMULATING PRIMARY ORGANIC GASTRIC DISEASES OR ACUTE PHASES THEREOF.

In these days of surgical alertness it must be borne in mind that acute surgical affections of the stomach may be simulated by a symptom-complex caused by disease elsewhere.

Cirrhosis of the Liver.—Gastric incidents in its course, as pain, vomiting and hemorrhage, acute in onset, may simulate gastric ulcer, with or without perforation.

Uremia.—Epigastric pain, vomiting, hemorrhage and collapse may occur, simulating gastric ulcer and perforation.

Locomotor Ataxia.—The gastric crises simulate acute gastric lesions and may appear like ulcer.

Gastric Neuroses.—The gastric neuroses of hysteria, neurasthenia and epilepsy simulate ulcer at times.

DIAGNOSIS.

Non-gastric diseases with gastric symptoms can only be recognized after an examination of all the organs of the body and a study of all excretions and secretions. The clinical course and the historical features are essential. The symptoms bear more or less relation to physiologic or pathologic fluctuations of the primary source of the disease, as of the eye, heart, kidneys, etc., and are not of the constancy of organic disease of the stomach. The gastric neuroses are inconstant as to character, irregular as to manifestation, both subjective and objective, and have a relation to emotional or psychic influences which require all the skill, genius and patience of the practitioner accurately to disclose.

FOOD STAGNATION FROM ALL CAUSES.

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When the stomach fails to empty itself within a reasonable time after the taking of food, this condition is termed food stagnation. It differs in degree, depending, in part, on the character of the food taken, still more on the morbid state giving rise to the condition. Semi-liquid or pultaceous food should leave the stomach in four or five hours, and if it is retained longer there is a certain degree of stagnation. An ordinary meal composed of a variety of foods is the proper test for food stagnation. With this meal the stomach should be emptied, according to Riegel, within seven hours, and the presence of contents beyond that time is evidence of food stagnation. There are conditions, however, in which the liquid food is retained for a much longer period than five hours, and solid foods are retained for twenty-four hours or longer. Under such circumstances, we have to deal with more serious cases.

ETIOLOGY.

Food stagnation is one of the most important of the gastric disturbances. It invariably gives rise to symptoms both local and general. Locally, the patient experiences distress and a sense of weight, sometimes pain, together with eructations of gas, regurgitation of the stomach contents, and often vomiting. In certain cases the stomach behaves in a lifeless, inactive manner; in other cases it takes on violent movements which the patient may feel and which the observer may perceive

through the abdominal parietes. Constitutionally, there are usually found evidences of autointoxication and starvation. These symptoms vary widely in different cases, depending on the degree of stagnation and on the character of the fermentation that may be present. The nature of food stagnation differs, as does its cause, and many conditions may lead to it. Cases may be roughly divided into two classes: First, those in which stagnation results from depression of the motor function of the stomach, without the presence of any actual obstruction. The stomach walls are simply too feeble to overcome the slight retention, or holding back, exercised normally by the pylorus. Second, those in which there is actual obstruction to the outflow of stomach contents, regardless of the kinetic energy of the gastric walls. There are certain cases in which we have to deal both with atony of the gastric walls and with obstruction at the pylorus. More often these cases begin with obstruction and the atony appears as a secondary matter.

Food stagnation is often associated with dilatation of the stomach, but on the other hand, there may be a large stomach without stagnation, and there may be very marked stagnation without gastrectasis. It is for this reason that Einhorn prefers to use the term ischochymia in the description of many cases formerly classified as ectasy, and it is this view which has led to the discussion of food stagnation as an entity; whereas, it was in former times almost invariably spoken of as an attribute of dilatation of the stomach.

Of the cases of the first class, anything which leads to the weakening of the muscular layer of the stomach may act as a cause. It, therefore, follows some cases of gastritis when the inflammation has invaded the muscle layers. It results from degeneration of the gastric muscle from any cause, and, therefore, occurs in grave anemias, inanition, severe intoxications and infections. It occurs in cases of great depression, more often when

this is prolonged, sometimes when it is brief, but acute, as in surgical shock, even though the stomach itself is not involved in trauma, or operation. I have known it to occur in acute illnesses without previous history of stomach trouble. Occasionally it appears to be congenital, and there are instances which seem to be hereditary and in which it occurs in a number of individuals of the same family. It may follow from adhesions to the stomach, thus making expulsive efforts ineffectual. It may result from imperfect innervation, and this may occur in consequence of general or local nervous depression. It most often results from overtaxation of the stomach; for instance, from eating or drinking excessively, especially the former, or from eating very coarse foods. This cause is naturally most operative when the functions of the stomach are depressed and systemic energy is on a low plane. The condition is, therefore, not infrequently induced by feeding abundantly too coarse food to convalescents. I have known it, for instance, to occur from overfeeding during or after typhoid fever. I knew a fatal case which followed the taking of a Christmas dinner by a convalescent from pneumonia. In every-day practice we most often find this type of food stagnation developing in people of lowered energy, such as is produced by overwork, mental or physical, excessive venery, etc., who at the same time are indiscreet in the quantity and quality of food taken.

As to the second class of causes of food stagnation, the most common is cicatricial pyloric stenosis, secondary to gastric ulcer. This sometimes arises from healed and sometimes from active ulcer, and chronic irritation or inflammation at the pylorus occasionally leads to the same result without the intervention of ulcer. There are a few instances in which we have to deal with benign hypertrophy of the pylorus with exaggerated action of the pyloric sphincter, giving rise to a palpable tumor and to disharmony between the detrusor and the sphincter apparatus of the stomach, the nature of which hyper-

trophy is not well understood. In some there is a congenital hypertrophy of the pylorus which may lead to fatal vomiting in the new-born, or later in life may develop into incoercible vomiting. A frequent form of obstruction is found in pyloric spasm, the result of oversensibility of the pylorus, either from erosions of the mucosa or simply from nervous hyperesthesia, more often associated with hypersecretion and hyperacidity of the gastric juice. In other words, the condition is found in gastrosuccorrhea and in hyperchlorhydria. The trouble may result from perigastritis with contracting adhesions, from band-like adhesions constricting the pylorus or duodenum, or from pressure exercised by tumors, or other processes, on these parts. The obstruction may occur some distance below the pylorus, thus giving rise to stagnation of the duodenal contents, as well as the contents of the stomach. Cancer of the stomach is a common cause of the conditions. Before a palpable tumor appears, there may occur spasm of the pylorus arising from its irritability. This may at first be transient in character, thus misleading the clinician. Gastroptosis, with the sharp bend in the pylorus or duodenum, is sometimes a cause, but its actual occurrence must be very rare.

MORBID ANATOMY.

The morbid anatomy of motor insufficiency of the stomach varies according to the nature of the case. In the early stages of gastric atony no change will be found in the structure. In advanced cases the stomach is likely to be found dilated, with more or less thinning of and, perhaps, fatty or fibroid degeneration of the muscle walls. The mucous membrane frequently shows the evidence of chronic gastric catarrh, with fatty or fibroid changes. When the stomach dilates, it is not always in the same direction, but is in the line of least resistance. More often the enlargement occurs around the greater curvature and fundus, although it may be at the antrum pylori or even upward toward the diaphragm.

DIAGNOSIS.

The diagnosis of stagnation is not difficult; it may be suspected when patients complain of eructations of food taken a long time previously. It can be demonstrated only by the use of the stomach tube. If the greater part of an Ewald test breakfast is found present three hours after eating, a moderate insufficiency is present, or if the stomach is not emptied seven hours after a hearty mixed meal the same conclusion is reached. The degree of food stagnation may be inferred from the amount of food found present; that is to say, if the stomach is found nearly empty, the insufficiency is small in degree; if, however, the greater part of the meal remains, the extent of the disability should be measured accordingly.

It is a good plan to examine the stomach in the morning, fasting. If the usual evening meal has been taken, and the stomach is found empty in the morning, the stagnation is not great. In most cases, in addition to the estimation of the motor insufficiency of the stomach, one passes to an examination to determine the size and position of the organ and to ascertain the state of the gastric chemistry. These features, while having an important bearing on the individual case, are not necessarily related to the food stagnation. Nevertheless, every case in which food stagnation occurs should have the most complete examination, not only in reference to the stomach, but to the organism as a whole. There is a very close relation between the systemic and gastric conditions.

TREATMENT.

The treatment of food stagnation or motor insufficiency is a broad subject and can not be fully discussed at this time. There are some principles which are so important that they should receive attention to the exclusion of details. In the first place it must be remembered that gastric atony may be but a part of a general atony, and gastric weakness but a part of general weakness.

On the other hand, there are cases in which the organism seems strong, but in which the motor power of the stomach is insufficient, and this without any unusual obstruction. Whether the atony is limited to the stomach or but an expression of the general debility, it is always of the utmost importance to manage the organism as a whole so as to increase energy and prevent its dissipation. In those cases where the stomach seems alone involved in the muscular weakness, local attention is, of course, especially demanded. The motor power may be assisted by certain mechanical measures, especially by really skillful massage over the region of the stomach, by trunk rotation and flexion, and by the alternate hot and cold douche over the epigastrium, and by external and internal faradization. The alternate hot and cold douching through the stomach tube has seemed sometimes to do good. As for drugs, undoubtedly benefit follows the use of the simple carminatives, bitter infusions, and temporarily the diffusible stimulants. These measures must be modified according to whatever other condition may be associated with the motor insufficiency; as, for instance, catarrhal gastritis, carcinoma, ulcer, ptosis, etc. It should here be reiterated that failure or success depends more on general management of the patient, on proper rest, exercise, recreation, diet, mental state, etc., than on the mere local treatment of the stomach. Of course, both must receive consideration.

Surgery has little place in this form of motor insufficiency. As for those cases depending on obstruction, surgical intervention is often of the utmost value; yet I can not agree with the dictum that all such cases are suitable to surgical relief. Where it depends on spasm of the pylorus from overirritability of tissue, whether from hyperchlorhydria, hyperesthesia, or simple erosion of the pyloric mucosa, surgery ought not to be considered; yet I have known these cases sent to the surgeon. There is no artificial drainage of the stomach which

compares in efficiency with the normal. The proper treatment consists in lowering the acidity of the gastric secretions, soothing the gastric mucosa and the selection of an unstimulating liquid or very soft diet which is free from all irritating particles. Lavage followed by soothing lavements of the mucous membrane is of great assistance. I have seen cases, which at first suggested serious organic disease of the pylorus, improve promptly under this treatment and know that the patients have continued without disturbance for years afterward. When there is ulcer at the pylorus, the question is more difficult. The present tendency, of course, is to operate at once, and ulcer of the pylorus is an ugly affair; yet in some cases in which the ulcer is small and yields readily to treatment it is probably wise to follow the conservative method, keeping the case for a while under observation before resorting to a gastroenterostomy. We are beginning to find out that a stomach on which a gastroenterostomy has been performed is by no manner of means as good as a normal stomach. If, however, the ulcer continues to give trouble, if pain and spasm frequently recur, I would recommend pyloroplasty (if the ulcer can be safely excised), otherwise gastroenterostomy. In benign hypertrophy of the pylorus without ulcer, I advise operation, preferably pyloroplasty. When there is cancer of the pylorus, excision followed by gastroenterostomy is probably, on the whole, the wiser course. If there is extensive involvement, gastroenterostomy alone often allows a year or more of comparative comfort to the patient. I have seen some brilliant results, but more depressing failures. Of the latter, it is only fair to say that by the operation there is little to be lost and possibly a year to be gained. In atonic cases, especially when associated with ptosis, some benefit follows from change of posture; and at times Rovsing's or other operations that raise the distended fundus, thus enabling the organ to drain, are of use.

Something should be said as to vomiting in this con-

dition. It is often a most conspicuous symptom, but varies much in its characteristics in different cases which appear to be of the same kind. Occasionally vomiting occurs only when the stomach is overdistended; at other times there are periods of great gastric irritability, with retching, even when the stomach is empty. In obstructive cases the nausea and vomiting often depend on yeast fermentation, and, with the exception of lavage, nothing gives so much relief as salicylic acid, which overcomes the yeast fermentation. Even when lavage is indicated, the relief afforded is greatly enhanced by the addition of this drug.

In closing this question of treatment, may I reiterate the feeling, which grows stronger the wider the experience, that it is impossible to expect the best results in dealing with this, as well as other stomach diseases, from purely special methods of treatment. The debt which we owe to those who have specialized in gastric diseases is immense, but the long-continued study of cases shows that, while we should avail ourselves of the art of the specialist, we can not dispense with the wide knowledge of general pathology and therapeutics which is the possession of the high-class general practitioner.

DISCUSSION.

ON PAPERS OF DRS. BILLINGS, DOCK, MUSSER AND STOCKTON.

Dr. Richard C. Cabot, Boston, asked Dr. Stockton on what grounds he would be willing to state, in any case, that there is an abnormal amount of mucus in the stomach contents. He also asked Dr. Musser if he could give any figures showing what proportion of all cases coming to him with stomach symptoms really have stomach disease.

Dr. G. W. McCaskey, Fort Wayne, Ind., declared that to say that in a certain sense the disorders of the stomach are fundamentally more important than those of other organs of the body is to utter the merest platitude. Gastric disease frequently stands in causal relationship to a large group of diseases, renal disease being among them. It is true that perhaps in the majority of such cases the intestines are the organs directly at fault; but if one traces the causes further back the ultimate cause will frequently be found to arise in gastric disease. Dr. McCaskey believes this to be true in a very large proportion of the cases. Abnormal gastric condi-

tions may lead to imperfect intestinal function. He emphasized in particular the necessity of a thorough comprehension of the physiology of the stomach before attempting to understand its diseases. This is not peculiar to the stomach, but in no other organ is it more fittingly illustrated. If, for instance, certain well-known facts regarding the physiology of the stomach had been taken into consideration, the dictum that the presence of hydrochloric acid excluded cancer would never have been made. There can be advanced cases of cancer of the pylorus (in which there are no acid-forming cells) without any diminution of the secretion of hydrochloric acid; in fact, it is liable to be increased at first as a result of the stimulation of the organ by the neoplasm. Many such cases have been reported, and Dr. McCaskey added one to the list within the last few months.* It seems to him that exaggerated conclusions have been drawn during the past few years in papers which have appeared on the subject of food stagnation. In one, for instance, an attempt was made to set the limit of twelve hours beyond which limit if food was found it indicated organic disease, in which operative interference was to be considered. In Dr. McCaskey's opinion much severer grades of gastric myasthenia are amenable to medical treatment. He is in accord with the conservative position taken by Dr. Stockton. Dr. McCaskey has found in a large proportion of the cases that intragastric cold douches do not agree with the patients. He does not know precisely why, but possibly it is because of the close proximity of the stomach to the solar plexus, or perhaps some peculiar susceptibility of the nervous organization of the stomach to the depressing action of cold. The importance of stomach analyses appears to him to be very great, and he endorsed and emphasized practically all that Dr. Dock has said. The recent attempts to belittle gastric chemistry are not well founded and are greatly to be deplored. He differed with Dr. Dock in the use of the Gunsberg reagent as a qualitative test for free HCl. He considers a 1 per cent. solution of resorcin much preferable because of its greater stability. Its delicacy is precisely the same, but no greater than that of the Guenzburg reagent. The questions of general nutrition discussed by Dr. Billings are of vital importance from the practical quite as much as the theoretical point of view. The problems of proteid metabolism are exceedingly difficult, and as yet are impossible of full solution. It seems quite probable that the existing dietetic standard with relation to proteid intake is somewhat too high, but just how much does not seem to Dr. McCaskey to be established. There is no doubt, however, that the nitrogen balance can be maintained and the organism kept in good working condition on much less than that indicated by the Voit standard, but it seems that we are not at present justified in accepting a standard

* THE JOURNAL A. M. A., April 1, 1905.

less than 80 grams of proteid per diem for the average individual of about 150 pounds weight. The investigations of Richardson and Folin are suggestive in the highest degree, even if their conclusions are not final, as it seems to Dr. McCaskey that the time over which the experiments ranged, even though of several months' duration, is not long enough to give final results. Even though body weight is maintained at a slightly lower level than before, and the working capacity of the individual remains up to the average, there are still other questions unanswered: the resistive power, for instance, of the individual to morbific influences; and the problem may even go further and be racial in its character. One fact should be clearly emphasized, and that is that the proteid intake should not vary with muscular exercise to the same extent as the carbohydrates. The latter are the force-producing, dynamic portion of the diet, and the quantity should rise and fall with the amount of muscular work done. The laboring man needs more starch and sugar and fat, but not necessarily a great increase in meat or other proteid foods.

Dr. Morris Manges, New York, said that the average general practitioners do not make extensive use of the valuable means of diagnosis at their disposal. Again, when such attempts are made, often the method is at fault, and especially is this true when an attempt is made to pass the stomach tube. Very often failure results because of the nature of the tube; the majority of these tubes are soft, and really can not be used by any one, and are often provided with a bulbous funnel at the ends. Another point is the awkwardness of the manipulator, possibly from lack of practice. As a result of all this, the general practitioner believes that these various methods of diagnosis and analyses of stomach contents, are too complex, though they are even simpler than the methods employed for urinary analyses. One need not bother with percentages; one only requires average figures. We must know relatively the presence or absence of free hydrochloric acid, etc. Another point Dr. Menges believes to be of importance is that what little of the stomach contents is found on the end of the tube can be utilized for diagnosis; no matter how small, strips of testing paper can be used by applying them to the end of this tube, and a complete analysis can be made. The futility of making one analysis should be emphasized. If we are dealing with organic disease the variations presented can only be appreciated by those who have worked with these tests; the use of one test breakfast will not do. It is positively absurd, he said, to depend on the results of one examination. By gross examinations of specimens one can determine a great deal in the vast majority of clinical cases.

Dr. S. P. Black, Pasadena, called attention to an important point brought out by Dr. Billings, i. e., the question of proper mastication. We all know that mastication is improperly per-

formed by all of us; if more time were devoted to proper mastication there would be far less bolting of food. When exercise is taken a meat diet is needed. It is necessary that mastication should be so complete that the gastric and intestinal juices may gain ready access to all particles of the food. If mastication is properly and thoroughly done, the appetite can be satisfied with a less amount of food. More that is taken in can be utilized and less will be excreted. The amount of food taken depends on so many conditions that it is difficult to state exactly the amount necessary for each. This varies with the period of life and many other factors. For instance, an old man can not take the same amount of food that a younger man can. It should be borne in mind that the majority of cases of chronic rheumatism are due to a toxemia from the decomposition of proteids. The excess of proteid material appears not only in the form of urea and other products, but also as ptomains which when absorbed give rise to chronic joint affections. The relation, therefore, between proteid intake and mastication can readily be seen and its importance recognized. Dr. Black quoted Dr. Stengel as saying that there exists a feeling among the profession that the examination of the secretion of the stomach is becoming of less and less importance and that an examination to determine the motor function of this organ is of prime importance. The papers read in this symposium place more reliance on the physiology of the stomach and a study of the stomach secretion. The laboratory is essential for a proper understanding of abnormal gastric diseases.

Dr. Joseph L. Miller, Chicago, asked what results Dr. Dock has had with Weber's test for blood in the stomach contents and what value he places on it. While it is true, Dr. Miller said, that in cases in which hydrochloric acid is present it is not absolutely necessary to test for pepsin, still in those cases in which there is an absence of hydrochloric acid it is necessary to determine whether pepsin is absent as well. He asked Dr. Dock if he resorts to this test. Dr. Miller believes this test should be in more general use. He believes that we should simplify exact qualitative determination more than we at present do. On the other hand, he also believes that a quantitative determination gives very valuable information. With Ewald's aspirator it is very easy to obtain all the contents of the stomach, and the use of this instrument simplifies the methods very much. When sarcinæ are associated with a marked increase in the hydrochloric acid, it is important as indicating a benign stenosis of the pylorus.

Dr. J. M. Anders, Philadelphia, said that it is a well established fact that physiology has a direct bearing on practice of medicine and is a most valuable aid in recognizing and treating diseased conditions. The only defect in this symposium is that the physiology of digestion has not been included. The

distribution of copies of papers such as presented by Dr. Billings would have a decided effect on medical progress in America. What Dr. Billings has given us is beyond dispute, and these things are most useful to the practicing physician. Dr. Anders was glad to hear him mention and emphasize the fact that the average amount of food ingested is at least twice as much as required to maintain complete physiologic efficiency. The minimum amount of alimentation necessary under the many varying conditions of life, including the ages of patients, is as yet imperfectly understood. The physician should be able, instead of as at present estimating empirically how much food is necessary, to determine this scientifically. The medical profession certainly owes much to the observations of Chittenden, Voit, Atwater and others. The determination of the amount of creatinin excreted daily is sufficient for the determination of the nitrogen balance of the body. Dr. Anders believes that up to the present time, and in the future as well, the most important advances will be those made as the result of analyses of food ingested and the urine, the feces, etc., excreted. In addition, it is necessary to take into consideration other factors, such as the influence of exercise, sleep and baths. These problems relating to the general nutrition are decidedly complex—more so than certain observers would have us believe. Dr. Musser has called attention to a long list of chronic affections in the course of which gastric symptoms may develop, but Dr. Anders would have been glad to have heard more regarding the development of gastric symptoms in the course of acute infections. Recently Dr. Anders saw a patient suffering from acute articular rheumatism, in whom the joint condition was in abeyance, with marked distension and severe acute pain in the epigastrium. It was naturally thought that acute gastritis or even perforation of the stomach might have taken place, but a careful physical examination of the patient revealed the presence of a plastic pericarditis. He had previously observed several instances in which the pain was referred to the epigastrium. Dr. Anders was pleased to hear Dr. Dock emphasize the variability in results from chemical examinations of the gastric contents. In his own experience, however, the variations in the chemical findings are less pronounced in organic affections of the stomach than in functional disturbances due to neurasthenia, and the like.

Dr. F. C. Shattuck, Boston, declared that there is too much theory regarding this matter. He believes that medical men are in danger of running after false gods. There are, he believes, but two conditions in connection with ulcer which call for surgery. The first is perforation; the other, obstinate cicatricial contraction of the pylorus.

Dr. James J. Walsh, New York, said that in stomach medication the nostrums have even a larger field than in any other

disease. Judging from the number of varying remedies for stomach symptoms of all kinds that are fairly pushed on the doctor by the advertising agents and the large amount of printed matter with regard to them that comes to his table, there must be an immense amount of medicine for stomach symptoms prescribed in this country. All sorts of ferments have been introduced and all the vegetable kingdom has been rifled of precious treasures in order to provide new stomachics. The more distant the country and the more unusual the plant from which they come the more grandiloquent the advertising and the greater the promise of efficiency. Josh Billings once said that it is not so much the ignorance of mankind that makes them ridiculous as the knowing so many things that ain't so, and there is no doubt that with regard to our knowledge of the stomach this is truer than with regard to almost any other department of medicine. Each individual is absolutely a law unto himself as regards his tastes and his capacity for digesting various articles. The distinguished Russian physiologist, Pawlow, has demonstrated that in animals at least a special kind of gastric juice is secreted for each kind of food that the animal takes. If to this be added the individual tastes in human beings and the psychic influence on the stomach, then the problem of stomach digestion becomes the most complex we know. Fortunately physicians do not have to bother much about the variations in the chemism of the stomach. So long as the stomach will pass on the food that is furnished it digestion will go on and will maintain nutrition. In cases of gastric cancer, for which the whole organ is removed, it is a common experience that the patients gain as much as 30 or 40 pounds in weight within a few months after the operation, in spite of the complete removal of their stomachs. This, however, is only a confirmation of what was known otherwise as the result of stomach investigation. Not a few persons suffer from achylia gastrica, that is, a condition in which there is no secretion of gastric juice in the stomach and no process of digestion carried on there, yet suffer very little from digestive symptoms and do not lose in weight. In more recent times the practice of jejunostomy has demonstrated the same thing. When there is a cancer of the pylorus and the patient has lost seriously in weight, digestion proceeds very happily and nutrition begins at once to improve when an opening is made by which food is allowed to pass on immediately to the intestines. Gastric motility, then, is more important than gastric chemism. If physicians can only switch the food past the stomach, the digestive system will continue its work. As a matter of fact, most of the tonics that do good in digestive disturbances influence the motility of the stomach rather than its secretory activity. That is why strychnin is so useful. The most serious difficulty that hampers stomach motility is the lack of proper mastication. Meats

must be chewed, but still more must vegetables be chewed. It is the vegetable-eating animals that ruminate. It is in this line and not in trying to help gastric chemism and the ferments that therapeutics are effective.

Dr. John A. Lichty, Pittsburg, believes that gastric atony due to organic obstruction is the crucial point in this symposium and that it will assume the same position in the next few years in the deliberations of this section that appendicitis did some years ago. After a rather extensive experience in the treatment of these conditions, he has found that in many cases he might have easily dispensed with mechanical devices, such as intragastric electricity, massage and lavage. Simply advising the patient to masticate his food more thoroughly and to refrain from drinking at meals and for an hour or two after seemed to be all that is necessary in many cases. Food not properly masticated must be ground up in the pyloric end of the stomach, and such extra work is likely to produce atony, erosion, ulceration or other gastric disturbances. Dr. Lichty did not mean to say that we should not use these agents in selected cases, for they are often absolutely essential to bring about a curve. In the treatment of gastric atony due to organic obstruction, the internist and surgeon must come together and understand each other. The earlier this is done the better for the patient's welfare. With the present methods of diagnosis physicians are not yet able to make a definite diagnosis in the earlier stages of some of the most important gastric lesions. The effect of rational treatment and the course of disease must be observed at times before a diagnosis can be made. Now and then it may be necessary to do an exploratory operation before a diagnosis can be made. Such an operation is not always a serious undertaking and may frequently reveal important conditions. Dr. Lichty recently saw a case in which he was positive that there was a gastric ulcer; the patient suddenly had an attack of jaundice and then he was positive that he had to deal with a case of obstruction of the gall ducts. There was found at operation a band of adhesion which interfered with the pyloric entrance and also with the gall duct. No amount of treatment would have relieved this patient, though she had received treatment from different physicians for a year or more for gastric ulcer and for gallstones. The tendency of the internist too often is to be satisfied to have patients in a chronic condition come to the office day after day until they are entirely dissatisfied and discouraged and ready to desert to the quack. There is still too wide a space between the internist and the surgeon, and in this space the quack and unscrupulous doctor find a rich harvest. The internist and surgeon must co-operate.

Dr. C. M. Cooper, San Francisco, said that Dr. Billings' paper should have been read before a conjoined section, inasmuch as the subject matter is unwisely neglected and its importance to all branches is equally great. It is not necessary

to tell the patient to limit the intake, as the muscular movements associated with thorough chewing plus the better digestion of the food chewed induce a feeling of satisfaction which in itself tends to diminish the amount eaten. Further, it must be remembered that a thorough clinical examination should come before a chemical analysis of the stomach contents. On the Pacific slope aneurism is so common—abdominal aneurism as well as thoracic—that such an inverted order of examination might lead to serious trouble. Moreover, frequent chemical examinations are just as important as frequent stomach-content analyses. If prior to the passing of the stomach tube the patient suck a strong English peppermint the throat is partially anesthetized and the proceeding is rendered less difficult in sensitive patients. Though, of course, periodic gastric crises may occur in locomotor ataxia and be due to that alone, sometimes there is a local trouble underlying or complicating the nerve storms, as in two cases which Dr. Cooper recently saw. In one there was stenosis of the pylorus; in the other, a band binding down the first part of the duodenum was demonstrated by operation. The great majority of physicians refer their gastric patients too late to the surgeons and terminal infections occur. Patients should be referred back to the physician; otherwise the primary constitutional tendencies which have led to secondary lesions necessitating surgical interference will often remain uncorrected.

Dr. Norman Bridge, Los Angeles, Cal., said that one important point in the physiology of the stomach has been omitted in this discussion, and that if physicians could keep this point in mind it would simplify the subject very much. The stomach is not useful in absorption. The important thing regarding this organ is its motility, and the purpose of the stomach seemed to be to act as a reservoir to receive and to retain food for a variable period of time and to deliver it slowly to the intestine. The stomach could be left out of consideration for the business of digestion. If we could get the food out of the esophagus, through the pylorus, it then would be possible sufficiently to nourish patients. The absorption of water even does not take place to any extent from the stomach. It is a convenience to mankind to take food into the stomach at certain intervals and to go on about the business of life. If one takes too much food and absorbs too much, it is the intestines that do it and not the stomach at all. Dr. Bridge thinks that it can be shown that the stomach may directly cause such systemic diseases as Dr. McCaskey has referred to.

Dr. Frank Billings, Chicago, stated that carbohydrates and fats furnish the animal body fuel. The proteid food furnishes the defect due to waste of the muscular system and other organs which perform the work for the body. The amount of carbohydrates and fats necessary for fuel for an adult will depend on the character of the work. A laboring man will require

more than a man who leads a sedentary life. The amount of proteid necessary to repair the waste from muscular exertion, etc., has been found to be only about one-half that which has been advocated for years in the standard dietaries. With this one-half the amount of proteids a nitrogenous balance may be maintained. There are fanatics on all subjects, and in this particular one those who advocate a very low proteid intake and over-mastication, as compared with ordinary chewing of food, may do things which appear ridiculous. Nevertheless, the action of these men and what has been written on the extreme side of the question by them has brought the attention of the public to the subject and in this way has been of great benefit. The lay public and many of the medical profession believe that all strength, nutrition and force comes from the proteids and especially from the albumin of meat. The fact is that the proteid is simply a tissue builder, and growing individuals, therefore, may require a considerable amount of albumin, but when the growth is once attained only that amount of proteid will be necessary to maintain good health and strength which will furnish food to take the place of the waste produced by muscular and other bodily activities. The amount of proteid necessary for each individual may differ, but only that amount will be required which will maintain a nitrogenous balance, as evinced by the nitrogenous output in the urine, feces, etc. Dr. Billings mentioned an error which may occur from the use of bread in a test meal. Sponge bread so used, even after twenty-four or more hours old, will show yeast cells in the stomach contents and may, therefore, be misinterpreted as indicating stasis of the stomach contents.

Dr. George Dock, Ann Arbor, said that he considers visible masses of mucus in the stomach contents as abnormal, but one must be sure this mucus does not come from the respiratory tract or from the mouth or be the result of awkward manipulation of the tube. On the other hand, a small amount of mucus which is visible may be present, and yet one can not say from this alone that the patient has chronic gastritis. Though the physician can not draw the line anywhere, Dr. Dock would say that in general more than from 3 to 5 c.c. is abnormal. He agreed that resorcin is an excellent test, but he likes Günsburg's better. He also agreed that not too much time should be spent in working with the decinormal solutions, etc.; but, on the other hand, a physician should have had practice with these before doing more rapid work. The examination of the vomitus he believes to be very important, but he sounded a note of warning against the use of this method as a substitute for the tube; it is a dangerous one. A patient can vomit a large quantity and yet the stomach contain still more important material. Dr. Dock has been using tests for occult blood in the laboratory, and with satisfaction. He has also looked for occult blood in the stools after excluding any bleeding points in the rectal mucosa. Delicate reactions for blood in stomach

contents are easy, but one may meet with many instances in which there is no distinct lesion of the mucous membrane. He agreed with Dr. Miller regarding the test for pepsin and also for rennin. They are useful, but one can very often get along without either of them. The presence of sarcinæ gives valuable information in many ways. Sarcinæ are rarely found in malignant disease of the stomach. If found in large quantities it is sufficient to say that the patient has not malignant stomach disease. On the other hand, yeast is often found in gastric cancer when hydrochloric acid is still present. He is not so enthusiastic with regard to the surgery of the stomach as Dr. Walsh. He agreed that cancer should be operated on if possible. In cases of ulcer, also, he has had patients operated on and with good results. But doing a gastroenterostomy in case of ulcer does not make the patient normal. In a large number of patients, 16 or 17, who have been reported as being operated on for gastric ulcer, peptic jejunal ulcers have developed which were even more dangerous than the original gastric ulcer. This ulcer tendency can not be cured by operation, and so it is with functional disease and stagnation of food; it has not been demonstrated in cases of gastroenterostomy or pyloroplasty that the stomach is as good as before. Therefore, he thinks, physicians should take the middle ground between what Dr. Walsh has given us and those who take the gloomy aspect or conservative aspect in regard to this subject.

Dr. Charles G. Stockton, Buffalo, thinks that lack of success is often due to the way in which cold is employed. If too cold, or if too much force is employed, depression is likely to follow. Sometimes benefit is to be obtained by alternating the cold with the hot douche. He also emphasized what Dr. Manges said regarding the importance of selecting a proper stomach tube. This is a point that is often overlooked. He also agreed with Dr. Lichty that in the treatment of stagnation, which depends on atony rather than on obstruction, much can be accomplished in attention to mastication and the withholding of liquids at meals. In any case of atony of the stomach reaching to stagnation, without obstruction, one should not forget what can be accomplished through the general management of the case and general measures. He advised physicians not to overlook general innervation. On the other hand, he said one often fails to obtain success because of overlooking local treatment. He disagreed with Dr. Bridge that the stomach is practically unnecessary. Physicians are too prone to say that certain organs are unnecessary to-day. He does not believe that one can get along without the stomach, even if anastomosis is practicable. In some cases of achylia gastrica the stomach will empty itself quickly, within ten minutes after a meal is taken, thus showing an enormous motor activity. This state may be compared to that of the patient without a stomach. Yet these cases of achylia gastrica have general and local symptoms and the victims are not well people.

COCCIDIOIDAL GRANULOMA.*

W. OPHÜLS, M.D.
SAN FRANCISCO.

We have in California a peculiar form of oidiomycosis of which, so far, no cases have been described in people who had not been in our state, except the very first case of this form of infection which was observed by Wernicke[1] in Buenos Ayres and later more accurately described by Posadas. The first case in California was reported by Dr. E. Rixford[2] of San Francisco to the San Francisco Medico-Chirurgical Society, March 4, 1894. Another similar case under the care of Drs. Thorne[3] and Robinson was seen by him[4] the same year. Later Dr. Rixford,[5] in conjunction with Dr. Gilchrist of the Johns Hopkins Hospital Medical School, gave a more complete description of these two cases and of the parasite.

This description established fully the morphology of the parasite in the tissues and the nature of the lesions which it produces. At that time, however, the organism was looked on as a protozoon, on account of failure to obtain growths, and on account of a certain resemblance to the coccidia named *Coccidiodides immitis pyogenes resp.*, the idea being that on account of some mor-

* From the Pathological Laboratory of Cooper Medical College, San Francisco.

1. Wernicke: Centralblatt f. Bact., 1892.
2. Occidental Medical Times, 1894, vol. viii, 326.
3. Thorne: "A Case of Protozoic Skin Disease." Occidental Medical Times, 1894, vol. viii, 703.
4. Rixford: "A Case of Protozoic Dermatitis." Occidental Medical Times, 1894, vol. viii, 704.
5. Rixford and Gilchrist: "Two Cases of Protozoan (Coccidioidal) Infection of the Skin and Other Organs," Johns Hopkins Hospital Reports, vol. i.

phologic differences the parasites in the two cases might not be the same. This view of the animal nature of the parasite proved to be erroneous in the course of the examination[6] of a new case of this disease which occurred in 1900, when it became apparent that the para-

Fig. 1.—Face lesions in Case 4. From article by Montgomery (British Journal of Dermatology, xii, 1900).

site could be cultivated and developed in the cultures in the form of a mould-like growth. It probably belongs to the oidia. I have therefore proposed the name *Oidium coccidioides.*

6. Ophüls and Moffitt: "A New Pathogenic Mould," Philadelphia Medical Journal, 1900.

The lesions as well as the parasite of coccidioidal granuloma show certain resemblances to the tissue changes and organisms found in blastomycetic dermatitis as described by Gilchrist, Stokes and Gilchrist, Wells, Hessler, Hyde, Hektoen, Montgomery and others. There is this difference, however, that whereas in blas-

Fig. 2.—Skin lesions on face and hand of Case 2. Taken from Rixford and Gilchrist's paper in Johns Hopkins Hospital, Rep., I.

tomycetic dermatitis the primary focus of infection always is the skin and the disease remains localized in that organ, with the exception of one case reported by Walker and Montgomery,[7] in which a generalization of

7. "Further Report of a Previously Recorded Case of Blastomycosis of the Skin; Systemic Infection with Blastomyces, Death, Autopsy," THE JOURNAL A. M. A., 1902, vol. xxxviii, 867.

the process took place; such generalization of the disease is the rule in coccidioidal granuloma and the primary focus of infection is just as frequently to be found in the interior of the body as in the skin. Typical cutaneous lesions are often missing entirely. The parasite in coccidioidal granuloma differs from the various fungi described in blastomycetic dermatitis first by the absence of budding during its development in the tissues, second by its multiplication by endosporulation, third by cer-

Fig. 3.—Face lesion from Case 3, second case of Rixford and Gilchrist (Johns Hopkins Hospital Reports, I).

tain differences in its growth on artificial culture media. Still the resemblances between lesions and parasites in blastomycetic dermatitis and those in coccidioidal granuloma seem close enough to my idea to classify them together, perhaps after Ricketts' suggestion, as oidiomycoses. It must be acknowledged, though, that there is this difficulty in the way of accepting Ricketts' nomenclature, namely, that under the term oidiomycoses should be included all diseases produced by oidia, whereas Ricketts attempts to limit the term to what is

commonly known as blastomycetic dermatitis, a few cases of more general infection with yeast fungi and infections with *Oidium coccidioides.* On the other hand, the term blastomycosis would hardly include all the fungi which cause these troubles. Many of them are very much more complicated in their modes of development than ordinary blastomyces. In this dilemma about names I believe we should look rather to the profes-

Fig. 4.—Nodules resembling tubercles and chronic miliary abscesses in pia mater of spinal cord in Case 7. Low power.

sional botanist than to the medical worker for a decision whether these organisms should be properly classified as blastomycetes or as oidia. Certain is this, that we have here a class of diseases usually with the anatomic characters of granulomata frequently localized in the skin but also occurring in other organs which is caused by a variety of lower fungi, some resembling more blastomycetes, others more oidia.

There are now on record 10 cases of coccidioidal granuloma, to which I can add three new cases, mak-

ing 13 in all.[8] Unfortunately, the records of the three new cases are not complete.

One of these is the case of a young canner, C. M., 19 years of age, who came to the City and County Hospital at San Francisco Sept. 23, 1901. Before entering the hospital he had irregular attacks of fever with violent chills for four weeks. In the hospital he developed the symptoms of a severe, unusually chronic meningitis and died Dec. 17, 3 months after entering. The necropsy showed an old calcified caseous spot in one of the peribronchial lymph glands on the left side, one old miliary tubercle in the left kidney, a chronic irregular caseous process in both adrenals, a basilar meningitis with many tubercles in the Sylvian fissures and a very extensive

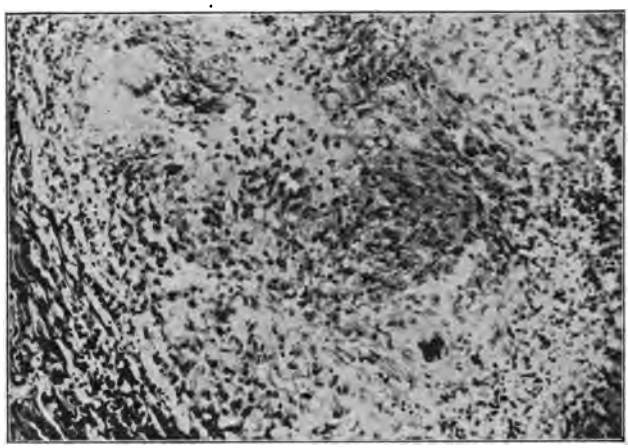

Fig. 5.—Nodules resembling tubercles. Pia mater of spinal cord, Case 7. High power.

chronic inflammation of the pia mater of the spinal cord which in places was 3 to 4 mm. thick and full of tubercles and submiliary abscesses. The spinal cord showed a marked softening especially in the periphery underneath the thickened pia mater. He also had a terminal bronchopneumonia and beginning cystitis and pyelitis in consequence of a paralysis of the bladder which developed toward the last and necessitated catheterization. At the time the case was regarded as an ordinary case of tuberculosis. No attempts were therefore made to obtain cultures. Several years later, only adult and

8. At the end of the paper is a short synopsis of the cases already published and a more detailed account of the new cases. The numbers in the text refer to the numbers given to the cases in that place.

sporulating form of *Oidium coccidioides* were discovered in sections from the meninges. One of the most remarkable features of this case is that tubercle bacilli and no other parasites were found in the adrenals, whereas no tubercle bacilli, but many oidia could be demonstrated in the meninges.

The second case was one observed at the German Hospital in San Francisco in Dr. Weil's service, to whom I am much indebted for allowing me to make use of it here. The patient was an old man, born in Germany in 1842. When 16 years old he had an enlargement of the glands of the neck with extensive suppuration, which after considerable time healed with the formation of large scars. He came to America in 1874, lived in New York, San Francisco, Oakland and Sacramento. He

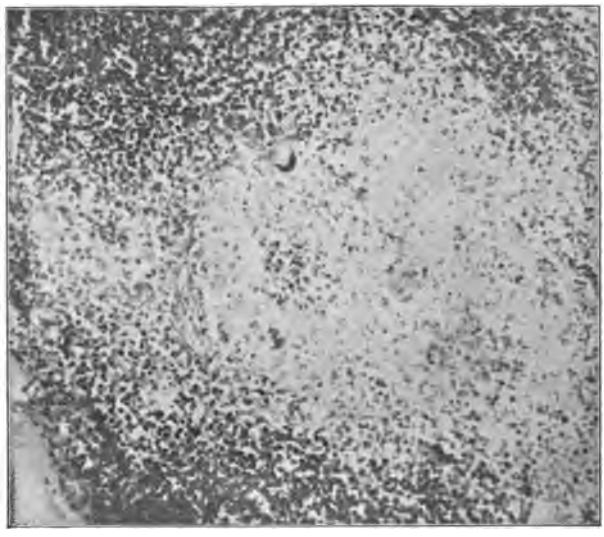

Fig. 6.—Tubercle-like nodule with small central abscess. Pia mater of spinal cord, Case 7. High power.

was employed most of the time as a baker or as a mill hand. In Sacramento he was overseer of a large market. He never lived in the San Joaquin Valley. Toward the end of 1903 a large cold abscess developed on the left side of his chest which was opened in March 1904. Two ribs were resected. The wound remained open ever since. Later soft fluctuating swellings developed on both sides of his neck. In June, 1904, Dr. Weil curetted the open sinus and removed some diseased bone. Microscopic examination of the granulation tissue showed miliary and submiliary chronic abscesses, some with giant cells in their walls and in these abscesses the parasites; there

were many sporulating forms. Some time afterward the patient was discharged, apparently cured.

In the third case, Chinese, W. D., at the City and County Hospital, the external condyle of the right humerus was removed in June, 1905, on account of caries involving the elbow joint. Microscopic examination of the specimen showed fibrous thickening and cellular infiltration of the periosteum and the adjoining muscle. There was extensive destruction of the bone with formation of tubercle-like nodules with large giant cells of the Langhans' type. In other places there were submiliary chronic abscesses. One section shows a large area of diffuse caseation. In the latter were many large full grown

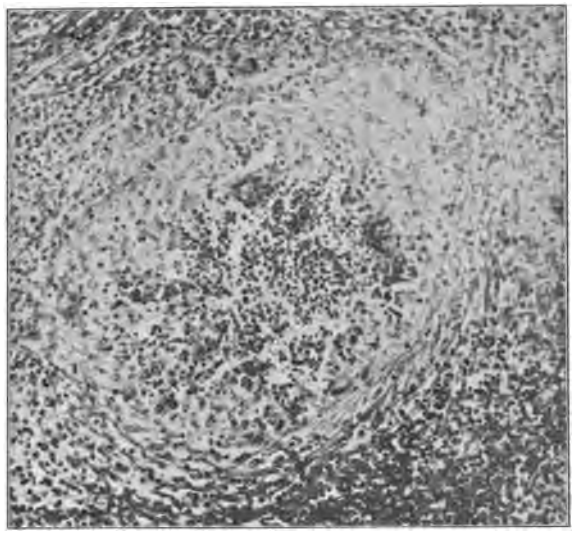

Fig. 7.—Chronic miliary abscess with giant cell in wall. Pia mater of spinal cord, Case 7. High power.

parasites. In one of the submiliary abscesses was a typical sporulating form. The patient died with symptoms of a chronic pulmonary trouble with sputum in which no tubercle bacilli could be found. He also had a paralysis of both legs. Unfortunately in this case also no necropsy could be made.

If we look over the cases so far reported in order to obtain a clinical and anatomic picture of the disease, we find that on account of the great variety of lesions produced by the parasite and the great variety of organs affected, it is very difficult to make any generaliza-

tions. The clinical symptoms in these cases, of course, depend entirely on the localization of the disease in the different organs of the body and the extent to which these organs have been involved in the process. So far no typical clinical picture can be given, but in some cases there is a striking resemblance to tuberculosis. In regard to the anatomic changes, one can say that the disease belongs to the infectious granulomata resembling tuberculosis, although at times differing from it in certain respects. As in all infectious granulomata the

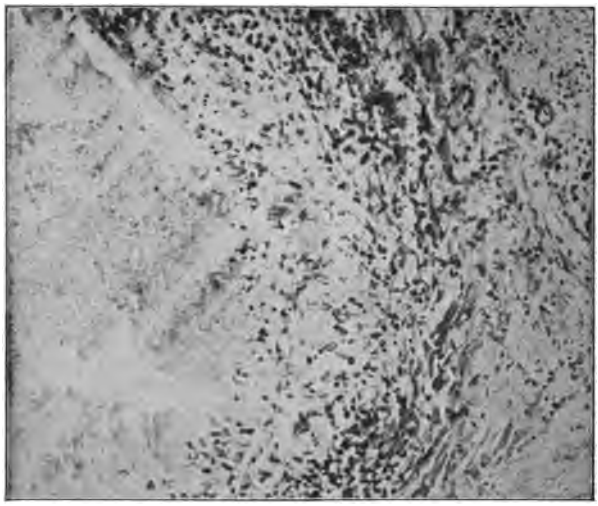

Fig. 8.—Large nodule with caseation. Pericardium, Case 6, High power.

manifestations of the disease are very manifold, the most characteristic, of course, being nodules consisting of granulation-tissue at various stages of development, but in addition to such lesions and mixed with them we find suppurative processes usually of a chronic character which in exceptional instances may be quite acute, however. The infection with *Oidium coccidioides* therefore produces either submiliary, miliary or larger nodules, which resemble tubercles very closely. These nod-

ules may caseate. Later the caseous material may liquefy and cavities containing pus-like material may be produced in this way. Or, in other cases, there may be suppuration from the beginning, sometimes of a rather acute type, but usually more chronic in character, leading to the formation of miliary or larger, sometimes very large (size of an infant's head) chronic abscesses or chronic ulcers. The lesions are nearly always progressive, with marked tendency to dissemination by the

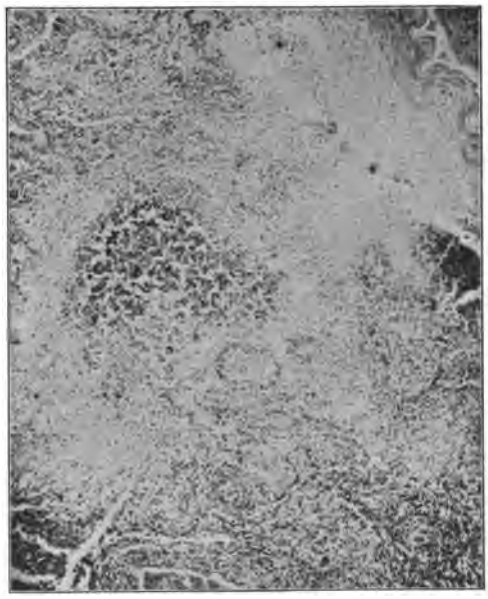

Fig. 9.—Subacute basilar meningitis with caseation in Case 6. Low power.

lymph and blood current, still sometimes they may heal eventually. In this tendency to rather rapid spreading in the same organ and from one organ to another, and in the more suppurative character of the lesions the disease at times resembles glanders more closely than tuberculosis, although it has been clinically most often confounded with the latter.

Six of the 12 cases which have been reported more ac-

curately had peculiar skin lesions. The appearance of these differed considerably in the different cases. Sometimes they were composed of large tubers with more or less ulceration, recalling the clinical picture of mycosis fungoides. This was observed in Cases 1 and 4.[8] The lesions in the latter case are shown in Fig. 1. In Cases 2 and 8 the nodules in the skin were much smaller and the trouble had the appearance of a hypertrophic lupus,

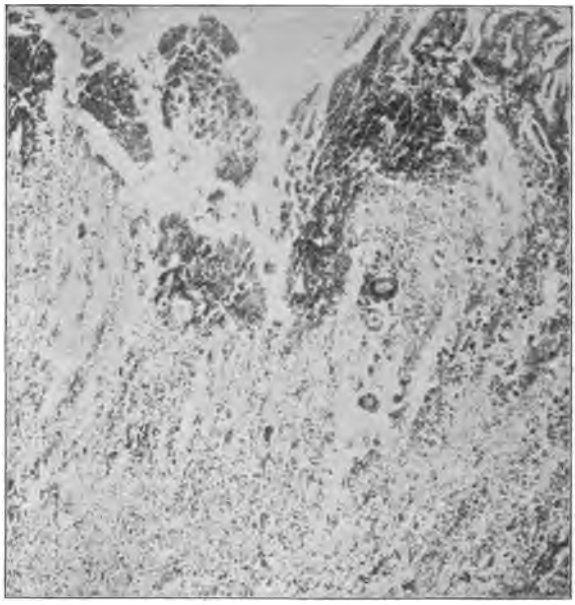

Fig. 10.—Wall of chronic abscess with many parasites, Case 5. High power.

as shown in Fig. 2. Again in Case 3, the lesions were more ulcerative in character, there was less tumefaction at the edges of the ulcers and instead of more or less solid nodules, submilliary abscesses were largely encountered (Fig. 3). The trouble in these cases usually started in some exposed part of the skin and extended from there discontinuously more or less all over the body. In one of my cases, a Japanese, there was only

one ulcer on the foot, of the appearance of a simple chronic ulcer without tumefaction, nodules or miliary abscesses at the margins. The ulcer was covered with a thick brown scab.

These cutaneous lesions seem to have been the primary seat of infection in 4 of the 6 cases. In Cases 4 and 8 this is a little doubtful, because in both of them there were symptoms of internal disease before the cutaneous manifestations developed. Case 4 apparently is an example of primary pulmonary infection, of which there are two more instances among my own cases. In Case 5 the first clinical symptom was a pleurisy on the left

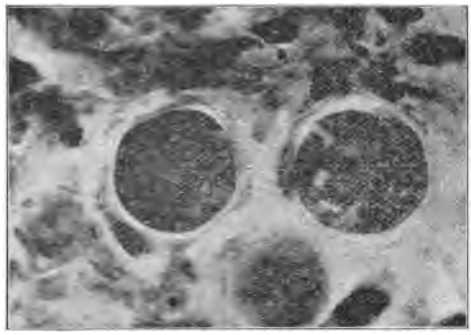

Fig. 11.—Adult parasites, Case 5, 1/12 hom. immersion.

side, and at the necropsy the lungs were found extensively involved. In the other, Case 6, there were old scars at both apices, from which the process probably had started. Case 7 also probably has to be regarded as a primary pulmonary infection; otherwise the source of infection would be entirely obscure in this instance, in spite of careful anatomic investigation. In the other cases there was no chance for investigation sufficient to obtain any clue in regard to the mode of infection.

In the lungs a variety of conditions have been observed. In Case 6 nothing was left in the lungs except small scars at the apices, whereas in other cases the lesions were rapidly progressive and very destructive.

Case 5, which is a typical example, showed irregular nodular consolidations, with extensive caseation and abscess formation, many disseminated miliary nodules and small abscesses, several large abscesses, one extending into mediastinum and another into the diaphragm. There was an empyema on the left side. The early involvement of the pleura and the extension of intrapulmonary abscesses into adjoining viscera (mediastinum, diaphragm, soft tissues of the lower neck, etc.) seem to be rather characteristic of the disease.

If the lungs are infected secondarily by the blood

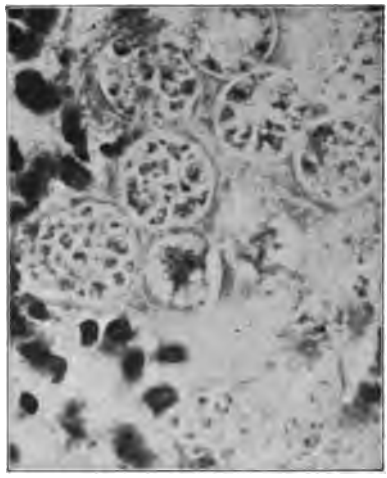

Fig. 12.—Sporulating parasites. Case 5, 1/12 hom. immersion.

current, the result, as a rule, seems to be the formation of innumerable miliary nodules, very much like those observed in acute disseminated miliary tuberculosis. These also occur in such instances in spleen, liver and kidneys and may or may not develop in these organs into small chronic abscesses.

The lymph glands are affected early and extensively. They usually show enlargement, caseations and suppuration.

In its predilection for certain organs the disease is rather similar to tuberculosis. The adrenals are fre-

quently diseased (mentioned in Cases 2, 7, 8). In all three cases the lesion consisted in an extensive caseation of these organs. Basilar meningitis, resembling tubercular meningitis very closely, was observed in Cases 6 and 7. In Case 6 the lesions were rather acute, like ordinary tubercular meningitis, whereas in Case 7 the process was very much more chronic, lasting for over three months.

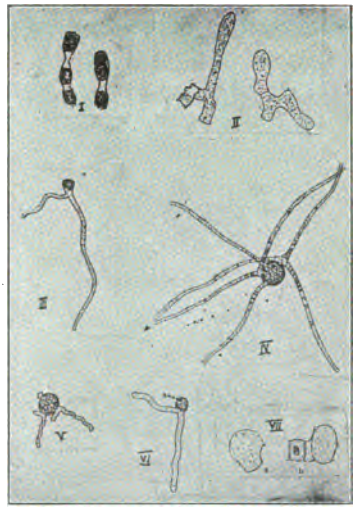

Fig. 13.—Development of parasite on artificial media. Taken from Ophüls paper, Jour. of Exp. Med., vi, 1905. I. Spores in ends of hyphæ. II and III. Germination of spores. IV and V. Development of hyphæ from spherical forms of parasites. VI. Development of hyphæ from spore formed by endo-sporulation in tissues. VII. Development of spherical forms in tissue from spores formed in cultures.

Disease of the bones was noticed in Cases 2, 5, 10, 11, 12. The trouble was often multiple and had the appearance of a chronic suppurative periostitis and osteomyelitis, with caseation. Here, again, in some instances particularly, the resemblance to tubercular caries was quite marked.

In one case only (Case 2) the internal genitalia were affected. There was a chronic caseation and suppuration of prostate, seminal vesicles, both epididymides

and testes. This observation is interesting on account of the invariably occurring chronic suppurative periorchitis in guinea-pigs after intraperitoneal injection.

The histology of the lesions is remarkable on account of the close resemblance of some of the lesions to those produced by the tubercle bacillus, showing that in tuberculosis, just as in all other diseases, the reaction of the tissues to the virus is not specific or in any way pathognomonic. In coccidiodal granuloma we also observe histologically interesting transitional stages between small

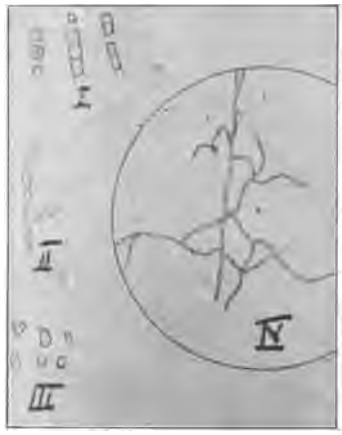

Fig. 14.—Development of parasite on artificial media. I. More unusual forms of sporulation. II. Yeast-like form found in old pure culture. III. Involution forms of spores. IV. Young mycelium showing septate and cylindrical hyphæ.

chronic abscesses and tubercle-like nodules, which, however, although more rarely, may also be found in cases of tuberculosis. Figure 4 shows, in one section "typical" tubercles, with giant cells of the Langhans' type and submiliary abscesses surrounded by thick layers of epithelioid cells. In Figure 5 several of the "tubercle"-like nodules are shown with the high power. In Figure 6 we see a similar nodule with a central abscess cavity filled with polymorphonuclear leucocytes, and in Figure 7 a chronic abscess surrounded by epithelioid cells. On

one side in the layer of epithelioid cells there is a small giant cell. Figure 8 is taken from the edge of a larger tubercle and shows typical caseation.

Examples of more acute lesions are given in Figs. 9 and 10. In Fig. 9 one sees an irregular accumulation of cells, largely polymorphonuclear leucocytes, in the meninges with beginning necrosis in places, and Fig. 10 illustrates the thick wall of one of the larger chronic progressive abscesses in Case 2. There is a thick layer of granulation tissue, the superficial layers of which are necrotic. In the granulation tissue there are many parasites; around some of them small abscesses are noticeable.

Fig 15.—Photograph of culture of *Oidium Coccidioides* on slanting agar-agar.

The *Oidium coccidioides* occurs in the tissues in the form of spherical bodies that grow to about 30 microns in diameter, consisting of an irregularly staining protoplasmic body and a double-contoured capsule which in the larger forms is thick and often covered on the outside with prickles or even long spines (Fig. 11). Different from the parasites in blastomycetic dermatitis, these spherical forms do not multiply by budding, but by endosporulation, as shown in Fig. 12. The formation of spores is preceded by a division of the protoplasm into 2, 4, 8, 16, etc., parts. The spores may number 100 and more. They are liberated by a bursting of the capsule and grow out directly either outside or often still within the old capsules into young spherical para-

sites. If many sporulating forms are present, the process is usually more acute and more suppurative in character. The number of the parasites in the lesions varies a good deal. Usually they are numerous enough to be easily found, at other times several sections have to be carefully studied before they are noticed. In pus they are most easily found when a drop of fresh pus is

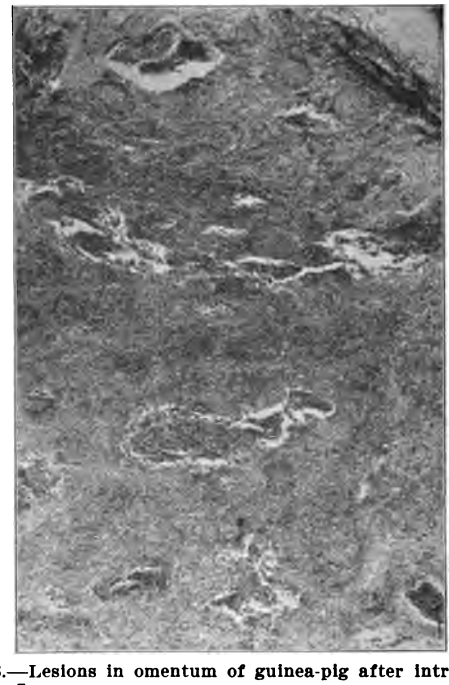

Fig. 16.—Lesions in omentum of guinea-pig after intraperitoneal injection. Low power.

spread between coverslip and slide and looked at with the low power.

When one of the adult parasites is placed in a suitable medium it grows out into long septate hyphæ in the manner shown in Fig. 13, iv and v, developing in course of time into a mouldlike growth (Fig. 15). It is probable that the spores also may be the starting point of such growth (Fig. 13, vi). It is not always easy to obtain the first growth, because not all parasites give rise

to the formation of hyphæ, and they do so only when they are free, entirely separated from the tissues. A drop of pus is the best material for starting a culture. Solid tissue containing parasites must be carefully teased or ground in a sterilized mortar before a growth can be obtained.

The fungus grows well on all media in the incubator and more slowly at room temperature. Fig. 14, iv,

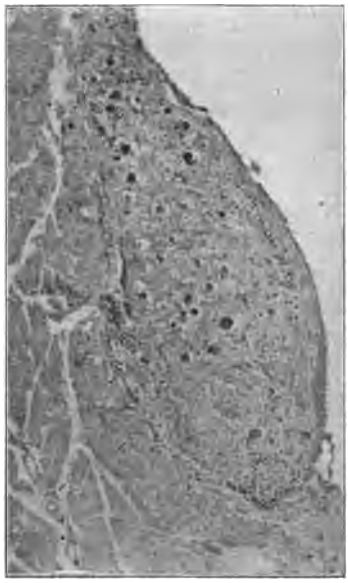

Fig. 17.—Nodule with many parasites on lower surface of diaphragm of guinea-pig after intraperitoneal injection. High power.

shows the mycelium of a fresh culture which consists of cylindrical septate branching hyphæ. After varying intervals, sometimes a month or more, spores develop in the ends of the hyphæ (Figs. 13, i, and 14, i). These spores are of interest, because from them, after introduction into the tissues, the spherical forms develop in the manner shown in Fig. 13, vii, by direct enlargement. As long as the culture does not contain any spores it is not infectious. Spherical forms with endosporulation are never observed in ordinary cultures nor

are mycelia ever found in the tissues. Wolbach, however, succeeded in developing the spherical forms with endosporulation outside the tissues in collodion sacs placed in the peritoneal cavity of animals.

The spores which form on artificial media can also be the starting point of a new growth on new media (Fig. 13, iii). The spores are first biconcave on both sides with sharp edges, later they may take all sorts of irregular forms (Fig. 14, iii). In old cultures I have found a few times yeast-like growths like the one shown in Fig. 14, ii.

Experiments have shown that dogs, rabbits and guinea-pigs are very susceptible to infection with *Oidium coccidioides*. The cutaneous lesions have been reproduced in dogs. Intraperitoneal injection is followed by chronic inflammation of the omentum with formation of nodules and abscesses, the formation of nodules on the peritoneum in liver and spleen and sometimes in pleura and lungs. In male guinea-pigs and rabbits, as has already been mentioned, a chronic suppurative periochitis develops after this form of infection.

After intravenous injection the chief lesions are encountered in the lungs in the form of innumerable miliary nodules; most other organs, however, are usually affected similarly and sometimes bone lesions occur. Fig. 16 gives an illustration of the lesions in the omentum of a guinea-pig. The microphotograph, which is taken with a very low power, shows numerous small abscesses in a mass of cicatricial tissue. In Fig. 17 a more tubercle-like lesion from the lower side of the diaphragm of an animal is represented.

So far it has not been possible to trace the source of the infection in any of the human cases. As mentioned before, the disease seems to be almost limited to California. Most cases have come from San Joaquin Valley, but some have been observed in people who have never been in that part of the country. There has not

been an epidemic outbreak in any place as far as is known. The cases have been found at considerable intervals in San Francisco in people coming from the country and had no apparent relation to one another. Several of the patients have been working as day laborers on the railroads, but not all of them, by any means. From what we know from the cultivation experiments it would seem quite possible that the oidium occurred in nature and caused infection occasionally only. Since animals are susceptible to it, it has been suggested that the trouble might be primarily an animal disease and only occasionally transmitted to human beings, but so far it has not been possible to adduce any evidence in support of this theory. I am fairly convinced that the cases are more frequent than would appear now. The resemblance of the disease to tuberculosis is so great clinically and anatomically that the true nature of the cases is recognized only when a careful microscopic examination is made of the diseased tissues or the pus from the lesions.

SYNOPSIS OF CASES.

CASE 1.—Case of Posadas and Wernicke (*Centralbl. für Bact.* 1892. *Revue de Chirurgie*, March, 1900, etc.) First symptom: appearance of bluish red tumor of size of lentil on right cheek, later large ulcerating nodules resembling mycosis fungoides appeared in various parts of the skin. Secondary involvement of regionary lymph glands. The disease lasted seven years. At autopsy disseminated nodular lesions were found in the internal organs.

CASE 2.—First case of Rixford and Gilchrist (*Johns Hopkins Hospital Reports*, I). Observed 1894. Male, 40 years old. First manifestation: sores on forehead and back of neck, later, disseminated cutaneous lesions resembling hypertrophic lupus. Nine years after first symptoms involvement of regionary lymph glands, death one year later. Lesions found in internal organs at autopsy: chronic abscesses, disseminated nodules, old scars and irregular areas of consolidation in lungs; chronic nodular pleurisy, nodules in diaphragm, circumscribed chronic nodular peritonitis underneath diaphragm and in pelvis, caseation and suppuration in peribronchial and retroperitoneal lymph glands, disseminated nodules in spleen, caseation of both adrenals, caseation and suppuration of prostate, seminal vesicles, both epididymides and testes, chronic

suppurative and caseous osteomyelitis of middle of left tibia and head of metacarpal bone of left index finger.

CASE 3.—Second case of Rixford and Gilchrist (*Johns Hopkins Hospital Reports*, 1). Observed 1894. Male, 33 years old. First symptom: two small pimples on forehead developing into chronic ulcers, later progressive disseminated ulcerative lesions of skin, early involvement of regionary lymph glands. Night sweats, remittent fever. Duration of disease 3 months. No necropsy.

CASE 4.—Case of Montgomery (*British Journal of Dermatology*, XII, 1900). Male, 21 years old. First symptoms: cough ten months before death. Two months before death appearance of large nodules resembling mycosis fungoides in skin over right eye which ulcerated, later widely disseminated cutaneous lesions. High remittent fever with night sweats. Secondary involvement of regionary lymph glands, rapid increase in pulmonary symptoms. Finding in internal organs at autopsy: large abscess in upper part of right lung extending underneath clavicle into soft tissues of neck. Several smaller abscesses and consolidated areas in right lung. Large abscess in right lobe of liver.

CASE 5.—Case of Moffitt and Ophüls (*Phil. Med. Jour.*, 1900, *Jour. of Exp. Med.* 1905, VI). A. L., male, 19 years old. First symptom: chill followed by pleurisy: later multiple arthritis, osteomyelitis of frontal bone. Slight chills and profuse sweating. Duration of disease: three months. Lesions found at autopsy. Irregular nodular consolidation with caseation and abscess formation in lungs, also disseminated miliary nodules, and larger abscesses extending into mediastinum and diaphragm. Empyema on left side, caseation and suppuration of retroperitoneal lymph glands, disseminated miliary nodules in liver, disseminated nodules and abscesses in kidneys and spleen, purulent periostitis and osteomyelitis of frontal bone, both tibias. Suppurative inflammation of both knees, right shoulder, both elbows and both wrists. Cultures obtained.

CASE 6.—G. B. (*Jour. of Exp. Med.*, 1905, VI.), old man. No clinical history. Lesions found at autopsy: Old partly healed lesions at apices, chronic nodular pericarditis, disseminated nodules in spleen and kidneys, basilar nodular meningitis.

CASE 7 (New case).—C. M., canner, 19 years, came to City and County Hospital, Sept, 23, 1901, had been in San Joaquin Valley for 12 days the month before, stopping at Bakersfield and Fresno. Before entering the hospital he had irregular attacks of fever with violent chills for four weeks. On entering he had high remittent fever, no plasmodia could be found, leucocytes normal, much headache, marked rigidity of neck. tenderness of cervical vertebræ, constipation. Kernig's symptom was present but not very marked. At intervals the

patient was in stupor or at times delirious. December 5, unequal pupils, complete paralysis of left abducens. December 6, paralysis of bladder. December 9, bed sores. He died December 17. At autopsy an old calcified caseous spot was found in one of the peribronchial lymph glands on left side, one old miliary tubercle in the left kidney, chronic caseation in adrenals (tubercle bacilli found in sections, no oidia). Basilar meningitis with many disseminated nodules in Sylvian fissures, very chronic inflammation of pia mater of spinal cord with thickening to 3-4 mm. in diameter. In thickened pia many miliary nodules and abscesses. Marked softening of cord. Terminal bronchopneumonia and beginning cystitis and pyelitis. The case was first regarded as an infection with tubercle bacilli. Later adult and sporulating forms were found in the meninges, no tubercle bacilli could be demonstrated in them.

CASE 8.—Case of Montgomery, Ryfkogel and Morrow (*Jour. of Cut. Dis.*, Jan., 1905). Findings at autopsy: Disseminated cutaneous lesions resembling hypertrophic lupus. No old lesions in lungs but many disseminated miliary nodules which were also present in spleen, liver and kidneys. Chronic caseation of adrenals. Cultures obtained.

CASE 9.—Japanese (*Jour. of Exp. Med.*, VI., 1905). Chronic simple ulcer of foot, caseation and suppuration of inguinal lymph glands and one of cervical lymph glands. This patient was later treated at the City and County Hospital in Dr. Huntington's service for a large abscess of the anterior abdominal wall which extended into the pelvis. The abscess was opened and drained. The patient discharged improved. It has been impossible to trace him since he left the hospital.

CASE 10.—Case of Gardner and Halton. An unusual infection in the bones of the foot. San Francisco County Medical Society, November, 1904. *Cal. State Journal*, 1904. Old man who worked on the railroad in the San Joaquin Valley. In 1900 he had an accident to right foot, followed by an abscess on the dorsum of foot. The abscess was opened and healed. Foot remained swollen and tender. In 1904 abscess formed over fourth metatarsal bone. It was freely opened and considerable necrotic bone and pale granulation removed. Curettings show caseation and formation of tubercle-like nodules. Many adult and some sporulating parasites. Amputation of foot. The patient is otherwise apparently in perfect health. Cultures obtained.

CASE 11 (New case).—D., patient at German Hospital, service of Dr. Weil. Male, German, born 1842. When 16 years old, while still in Germany he had an enlargement of the glands of neck with suppuration which after considerable time healed with formation of large scars. He came to America in 1874, lived in New York until 1877, then came to San Francisco, where he stayed until 1880. Then he moved to Oakland remaining there until 1897, when he moved to Sacramento. He has never lived in the San Joaquin Valley. He

worked as baker, millhand and in Sacramento as overseer of large market, where he had to handle poultry, rabbits, etc. Does not remember having seen many diseased animals. Toward the end of 1903 a large cold abscess developed on left side of his chest which was opened in March, 1904. Two ribs were resected. The wound remained open ever since. Large soft fluctuating swellings developed on both sides of his neck. Dr. Weil curetted the open sinus and removed some diseased bone. Microscopic examination of the granulation tissue showed miliary and submiliary chronic abscesses, some with giant cells in their wall. In these abscesses the parasites were found. Many sporulating forms. Cultures obtained.

CASE 12 (New case).—Chinese patient, of City and County Hospital, June, 1905. The external condyle of the right humerus was resected for caries which involved the joint. Microscopic examination of the specimen showed fibrous thickening and cellular infiltration of the periosteum and adjoining muscle; extensive destruction of bone with formation of granulation tissue full of tubercle-like nodules with large giant cells of Langhans' type. In other places there were submiliary abscesses. One section showed a large area of diffuse caseation. In the latter many large adult parasites and some empty shells. In one of abscesses a typical sporulating form. The patient suffered from a chronic pulmonary trouble with much purulent expectoration, no tubercle bacilli could be found. There was also a paraplegia of both legs. The patient spoke Chinese only, so no history could be obtained. He died within a short time, but unfortunately no autopsy was obtained.

CASE 13.—Parasites described by Wolbach, *Journal of Medical Research*, XIII., 1904.

DISCUSSION.

DR. H. A. L. RYFKOGEL, San Francisco, said that Dr. Ophüls has seen 12 cases in such a short time because he was looking for them. It may be demonstrated later that in California and in certain other parts of the universe the disease is fairly prevalent. Dr. Ryfkogel mentioned a case in which he was able to make the bacteriologic diagnosis. The clinical diagnosis had been made previously by Dr. Montgomery. For a number of years the case had been diagnosed as one of tuberculous disease of the skin. At first, Dr. Ryfkogel was not able to find the parasites in the cultures, and Dr. Flexner and Dr. Opie also tried to get them, but failed. Finally, Dr. Ryfkogel succeeded in finding them, as he realized after studying the sections made by Dr. Montgomery that the parasites were in the dense fibrous layers of the skin, and that none was on the surface. He found that in this case it was impossible to produce the disease experimentally by subcu-

taneous injections. Dr. Ophüls had the same experience with the cases he studied. It was easy to inoculate animals intraperitoneally. Of 100 animals inoculated, all developed caseous abscesses in all parts of the body, but only two out of the 100 developed pulmonary symptoms. These two died of miliary coccidioidal tuberculosis of the lungs, none of these abscesses being present. The original case suddenly developed symptoms that led to a diagnosis of pneumonia, and from this complication the patient died. There were no bone lesions, but the skin lesions were very extensive. There was enlargement of the suprarenal capsules with caseation, the size being that of a large orange. There was an acute miliary tuberculosis of the lungs, due to the fungus, not to the tubercle bacillus.

THE VALUE OF VARIOUS FORMS OF HEMOGLOBINOMETERS TO THE GENERAL PRACTITIONER

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AND
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We have undertaken this study because the general practitioner as a rule looks on hemoglobin instruments in general as a sort of medical toy, to be used largely by the consultant, and because we believe that the use of these instruments is practicable and that it does not take more time, nor nearly as much time with some forms, as is wasted over every patient by each of us.

In 1899 one of us read a paper before the Pennsylvania Medical Society in which the following points were noted:

1. The necessity of blood instruments becoming part of the equipment of every practitioner.
2. The value of various blood examinations as pointing out the true diagnosis and treatment in many cases.
3. The fact that blood examinations done in a routine manner do not take more time than is constantly wasted in gossip with each patient.

We believe these points were well taken and that they are daily becoming better recognized. In order that we may have certain grounds for the choice of the particular instrument to be used we undertook the study of the Fleischel, the Dare and the Tallquist hemoglobin scale. The Oliver was not studied because the three instruments named above are the most widely used in this country and seem to be all-sufficient. The descrip-

tions of each instrument and directions for their use can be found in all of the text-books on blood technic, and the reader is referred to them for information.

The studies were made mostly in the wards of St.

COMPARISON OF ESTIMATES BY DIFFERENT INSTRUMENTS.

Case.	Examiner.	Fleischel.	Dare.	Tallquist.	Gowers.	Case.	Examiner.	Fleischel.	Dare.	Tallquist.	Gowers.
1.—	M.	88	82	80	85	27.—	M.	78	86	80	..
	F.	80	84	80	80		L.	80	84	80	..
2.—	M.	80	76	80	80	28.—	M.	90	90	90	..
	F.	82	76	80	82		F.	88	92	90	..
	C.	76	74	80	80		H.	84	93	..	..
3.—	M.	82	84	80	84	29.—	M.	80	80	80	..
	F.	88	82	80	84		F.	82	84	75	..
4.—	M.	84	86	85	80	30.—	M.	82	88	85	85
	F.	88	86	85	88		F.	80	84	85	85
5.—	M.	76	72	75	75	31.—	M.	64	68	65	65
	F.	70	72	70	75		F.	66	68	65	68
	H.	80	74	70	78		L.	62	66	65	65
6.—	M.	40	42	50	..	32.—	M.	80	82	85	75
	R.	40	42	50	..		L.	78	84	85	75
7.—	M.	90	90	60	..	33.—	M.	72	73	75	74
	F.	88	85	70	..		F.	78	74	75	74
8.—	M.	87	90	90	..		L.	70	72	75	78
	H.	86	88	85	..	34.—	M.	80	80	85	82
9.—	M.	92	94	95	..		F.	84	82	85	84
	L.	84	85	86	..		S.	88	81	85	84
10.—	M.	82	75	80	..	35.—	M.	88	86	85	85
	L.	86	80	80	..		F.	92	86	85	86
11.—	M.	42	60	50	..		S.	96	86	85	86
	L.	45	60	45	..	36.—	M.	54	52	50	..
12.—	M.	65	65	65	..		R.	56	50	50	..
	R.	65	65	65	..		L.	50	52	50	..
13.—	M.	72	76	85	..	37.—	M.	62	58	60	..
	R.	74	78	75	..		L.	60	58	60	..
14.—	M.	84	85	85	..	38.—	M.	72	79	70	..
	R.	83	86	85	..		L.	74	79	70	..
15.—	M.	86	88	85	..	39.—	M.	80	75	80	..
	R.	85	88	85	..		H.	86	84	80	..
16.—	M.	72	74	75	..	40.—	M.	80	83	80	..
	F.	72	75	75	..		H.	82	85	80	..
	S.	76	80	75	..	41.—	M.	50	52	50	..
17.—	M.	72	74	75	..		H.	55	54	50	..
	F.	72	75	75	..	42.—	M.	65	60	65	..
	S.	76	80	80	..		H.	65	64	65	..
18.—	M.	82	86	80	..	43.—	M.	86	85	85	87
	F.	80	83	80	..		F.	82	85	85	87
	S.	82	84	80	..	44.—	M.	78	75	75	78
19.—	M.	76	78	80	..		F.	78	74	75	76
	L.	74	78	80	..	45.—	M.	83	84	85	84
20.—	M.	52	58	60	..		F.	79	84	80	86
	L.	58	56	60	..	46.—	M.	79	78	75	78
21.—	M.	78	76	80	..		F.	72	76	75	74
	L.	76	76	80	..		S.	75	78	75	76
22.—	M.	77	73	75	..	47.—	M.	88	86	85	86
	L.	72	75	70	..		S.	82	86	85	84
23.—	M.	70	74	70	..	48.—	M.	84	82	85	85
	L.	73	76	75	..		S.	80	82	85	84
24.—	M.	65	63	60	..	49.—	M.	86	80	85	82
	L.	67	65	65	..		F.	82	84	85	82
25.—	M.	40	38	40	..	50.—	M.	73	72	65	60
	B.	38	38	40	..		F.	73	70	65	65
26.—	M.	76	80	80	..		F.	73	68	65	64
	L.	80	82	80	..						

Timothy's Hospital, Roxborough, Philadelphia. Fifty cases were studied with each instrument. Each case was studied at the same time with separate instruments. Recognizing that the personal element could play a part in the reading of any one of the instruments, because a given individual might more readily use one instrument than another, the observations were always made simultaneously by at least two individuals and frequently by three, and the results compared. Dr. Marcellus was used as the basis of comparison in all the cases and his observations are found in each estimate.

In the Tallquist readings the percentage is frequently estimated at 85, that is, between 80 and 90; or 75, between 70 and 80.

In order that an individual might not be prejudiced in the use of any given instrument, the reading was done in the following manner: First the blood was examined by the Fleischel, the scale being covered. Then the Dare instrument was used and the scale was not consulted. Finally, the Tallquist was used. This was done because the scale of the Tallquist is always before the observer. If a known percentage is present, one is very apt to deceive himself in the use of an instrument afterward in the same case. The reading of each instrument was then noted and the results compared.

DIFFERENCES IN THE READING OF THE DIFFERENT INSTRUMENTS WHEN USED BY A SINGLE INDIVIDUAL.

Fleischel and Dare: 6 4 2 2 4 2 0 3 2 7 18
0 4 1 2 2 2=61 .....Average 3.3
Fleischel and Tallquist: 8 0 2 1 1 10 30 3 3
2 8 0 3 0 1 3 3=69.
Dare and Tallquist: 2 4 4 1 3 8 30 0 1 5
10 0 1 1 3 1 1=75.
Dare and Gower: 3 6 0 6 3 3 3 7 1 2 1 2
3 0 0 2=40.
Fleischel and Dare: 4 2 6 2 4 4 2 2 4 12 0
0 6 4 2 1 0 2 2=65.
Fleischel and Tallquist: 2 6 8 2 2 0 5 0 4 2
0 0 3 1 5 3 5 4=55.....Average dif., 3.1
Dare and Tallquist: 2 2 2 2 4 3 2 0 6 0 0
3 3 3 2 5 1=46.
Dare and Gower: 5 2 8=15 .....Average dif., 3.4
Fleischel and Dare: 4 7 5 3 2 5 1 3 1 1 2
2 6 1=39.
Fleischel and Tallquist: 2 2 0 0 0 0 1 3 2 4
3 1 1 8=27.
Dare and Tallquist: 2 9 3 3 2 5 0 0 1 3 1
3 5 7=44. .....Average dif., 3.3

In the fifty observations made by a single individual the variations seem to be very slight, indeed. If the reading is done with the Fleischel and Dare, the average difference in fifty cases was 3.3 per cent., with Fleischel and Tallquist 3.2 per cent., with Dare and Tallquist 3.3 per cent.

PERSONAL DIFFERENCES IN READINGS OF GOWER, DARE, FLEISCHEL AND TALLQUIST (MARCELLUS AS STANDARD).

Tallquist:		5	0	0	0	0	5	0	0	0	0	0	0	0	0
	0	0	0	0	0	0	0	0	5	0	0	0	0	0	0
	0	0	0	0	0	0	5	5=0.5.							
Fleischel:		8	4	4	8	6	4	0	2	8	1	12	4	0	0
	2	2	1	0	4	0	4	0	2	2	6	2	5	3	6	4
	4	0	0	2	2	4	2	2	2	2	2	2	2	6	2	4
	8	4	8	2	4	2	2	6	2	5	3	4	0	4	7	4
														Dif. 2,9 per cent.	
Dare:	2	2	2	0	2	0	5	2	1	15	0	0	2	2	0	1
	2	2	2	6	1	6	1	3	2	0	2	0	2	2	2	0
	2	2	2	4	4	2	0	2	2	1	1	1	2	2	0	0
	0	0	1	2	2	4	4	0	1	0	2	0	0	0	2...	
															1.85 per cent.	

The personal differences in the use of the different instruments is also seen to be extremely slight. With the Dare the difference was 1.85 per cent, with the Fleischel 2.9 per cent., with the Tallquist 1 per cent. It is fair to state that the Tallquist shows a less percentage of personal differences, because there is no opportunity to judge of less than 5 per cent. difference. The greatest personal differences were with Dare, 15 per cent.; with Tallquist, 10 per cent.; with Fleischel, 8 per cent. The readings of the Tallquist scale were the same in 78 per cent. of the cases, in Fleischel 0.5 per cent., in the Dare 22 per cent. It will therefore be seen that the readings by different individuals is least likely to be just the same with the Fleischel instrument, but, as shown above, the differences are so slight that this is not a fault which interferes with the practical use of the instrument.

It will, therefore, be seen that, so far as practical purposes are, any one of the three instruments is sufficient.

The Dare and the Fleischel allow of more accurate fractional reading because of the arrangement of the scale. All of the scales are accurate.

It appears to us that the advantages of the various instruments may be fairly stated as follows: Of the Tallquist scale, first, the cost is much less, $1.50; secondly, the bulk is less, it may be carried in the inside coat pocket at all times without inconvenience.

The first advantage of the Dare and of the Fleischel is that both can be used either by day or night. The Dare is less bulky than the Fleischel and does not need a particularly darkened room for its use.

The greatest disadvantage of the Tallquist is that one is forced to use it in daylight. The second disadvantage is that an accurate observation can not be made between the multiples of ten, and one therefore feels less sure of the result. The disadvantages of both the Dare and Fleischel are, first, the cost (about $20), and, second, the bulk, though the Dare is less bulky than the Fleischel. In conclusion, we may say:

1. Any one of the instruments studied by us is sufficiently accurate for practical purposes.

2. No practitioner should neglect to use one of these instruments. The Tallquist scale is cheap and convenient.

3. The Tallquist scale can be used for routine observations, and either of the other instruments for detailed and more accurate work.

4. The Dare instrument is just as accurate as the Fleischel, and takes much less time to manipulate.

5. For the general practitioner, the value of these instruments may be fairly arranged as Tallquist, Dare and Fleischel.

SYMPTOMS, DIAGNOSIS AND PROGNOSIS OF UNCOMPLICATED INTESTINAL AMEBIASIS IN THE TROPICS.

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SYMPTOMATOLOGY.

The symptomatology of amebiasis varies more than is generally taught and it seems desirable that this more comprehensive clinical picture be taken up more in detail, calling particular attention to the early diagnosis of the disease and to some of the peculiarities of the milder forms.

In discussing this question, writers have generally divided the cases into groups according to the clinical manifestation which, as clinical conveniences, answer the purpose and are fairly uniform. Osler considers it under the headings acute and chronic. Harris divided the disease into very mild forms, moderately severe cases and very severe ones. Lafleur and Futcher divide them into grave and gangrenous forms, those of moderate intensity and chronic ones.

I shall discuss the subject under the following convenient clinical divisions:

1. Latent and masked infections.
2. Mild and moderately severe ones.
3. Severe cases, including gangrenous and diphtheritic ones.
4. Infection in children and in the aged.

These clinical forms often change from one to the

other and may do so several times during the course of the disease in the same patient. The amebic process in all is essentially chronic, but acute symptoms from concurrent or secondary infection by other agents are frequently seen.

Latent Infections.—By this term are designated those cases in which there is a true pathologic process, containing amebas without diarrhea or other symptoms which would ordinarily indicate the presence of such an infection.[1]

It might be objected that this latency is really a period of incubation. In a sense, this may be true, but as many of the cases, even fatal ones, always remain in this class, and as there are nearly always certain manifestations in addition to the positive one of the presence of amebas, it seems better to give latency a separate place in the clinical classification; and, furthermore, the most useful results will be secured by making such divisions rather sharp and by confining the incubation period in all classes of the disease to the unknown time between the infection and the appearance of amebas in the stools.

Under these circumstances it is readily seen how difficult latency may be to differentiate from what properly may be termed incubation. This becomes all the more difficult when we remember that amebas may possibly be found transiently in the normal intestine and that there are at present no practical means of differentiating between species of amebas. It is clear, therefore, that by basing treatment on the method of diagnosis recommended, unnecessary therapeutics may occasionally be instituted.

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1. Dock, in 1891, reported extensive amebic ulceration in the cecum of a man who had not had dysentery and who had passed only normal stools. Councilman and Lafleur, in 1892, and Lafleur, in 1897, called attention to the fact that an amebic process may be latent, the stools being well formed and no amebas being found in the small adherent flakes of mucus, and that in these cases the true nature of the disease is often not suspected until abscess of the liver calls atention to it. These observations have been confirmed by Osler, Rogers and many other writers.

Cases of this latent class are not infrequent in Manila and are becoming more and more recognized, as we learn more of the character of the infection, and I do not believe that giving them a place in a purely clinical classification can be criticized by those who have had experience with the disease in the tropics. They are certainly of very great importance and deserve the most careful consideration, for the life of the patient often depends as much on the diagnosis and treatment here as it does in some of those clinically more active infections. Some of these patients, as has been noted, never show clinical manifestations during life, and in some others, when such symptoms do develop, the time for successful therapeutics may have passed.

The course and outcome, as in some other types, varies greatly. Usually, after a period ranging from a few weeks to many months, more active symptoms develop and in general the patient assumes the clinical type of a more or less severe dysentery. This change may occur gradually or very suddenly, and in the latter instance, unless the patient has been under very close observation, we may be misled into believing it to be one of primary acute amebic dysentery. On the other hand, some of these cases go on to recovery or death, without ever showing active diarrhea.

The symptoms during latency may be entirely absent subjectively and objectively for considerable periods of time; but usually conditions develop, which, by the aid of postmortem findings, we have come to recognize as indicating the nature of the process. As has been stated in previous publications, these cases are essentially those in which the lesions are in the cecum and upper colon. Careful stool examinations, obtained after a hydrogogue cathartic, often show mucus mixed with old discolored blood and other tissue elements, indicating both the location, and with their associated amebas, the nature of the infection. Rather indefinite, dull, aching abdominal pains are frequent and are often attributed by the

patient to "taking cold," because they are first noticed during the night or early in the morning, and afterward are usually most active at these times. There may also be some "indigestion," lassitude, headache, a coated tongue, foul breath, etc. Loss of appetite may be present, and the patient often notices slight loss of weight, and, if a woman, usually complains of loss of color and a yellow skin. Physical examinations will usually secure additional data. Deep palpation discloses tenderness along the colon, most often over the cecum, and if the duration is great and the patient not too fat, a thickened intestine may be made out.

Examples of this class of cases, as stated above, have been reported by several writers, and I have called particular attention to them in previous publications. Two additional examples from many that might be given are briefly as follows:

CASE 1.—A young married woman, previously in good health, came to the Philippines in 1903. About three months later she consulted me, complaining of general lassitude, dull pains in the back of the head and neck, coated tongue and bad breath.

Treatment.—She was given calomel and soda in broken doses, followed by a Seidlitz power the following morning, when examination of the stool showed amebas fairly numerous and of good size. She was placed on a bitter tonic of iron, quinin and strychnin. For the next three months there was little change in the general health and the bowels continued regular. Amebas were again demonstrated in the stools and this time were mixed with mucus, showing streaks of old discolored blood.

Course of Disease.—During the next month she complained of dull abdominal soreness, which on pressure was more marked in the region of the cecum. "Indigestion" was complained of, anemia was noticeable, and she had lost five pounds in weight; but the bowels were still regular and apparently normal. At this time she consented to take enemas, but after about a week's time she became dissatisfied and passed to the care of another physician, on whose recommendation she spent three months in Japan. While in that country her symptoms of indigestion were less noticeable and headaches were absent, and she returned feeling in better health and spirits. Shortly after her return to Manila, however, there was a recurrence of the symptoms before complained of, and in a more pronounced form; in addition flatulence became annoying; but there was still no diarrhea. Stool examinations after a

hydragogue cathartic showed numerous amebas, and considerable mucus with some blood. Her symptoms, as usual, were relieved temporarily by the cathartic. About this time she had had a moderate diarrhea, which lasted for a few days and was followed by constipation, with severe pains in the right iliac region. Another attack of diarrhea came within a week and dysenteric feces began to be voided. Typical acute dysentery developed, and death occurred within ten days after the acute onset and nearly one year from the time when amebas were first found in her stools.

Autopsy.—At necropsy an old advanced amebic infection of the cecum and upper colon, with most extensive ulceration and chronic fibrinous adhesions were found. More recent amebic lesions were scattered throughout the rest of the colon, and an exquisite acute diphtheritic dysentery was engrafted on the older process.

CASE 2.—A Filipino prisoner in Bilibid prison showed amebas in his stools on repeated examinations for more than four months. Sometimes after administration of salts blood cells were present, and the mucus was sometimes stained with dark, partly decomposed blood. He was apparently a perfectly healthy man, and had no diarrhea or dysentery.

Autopsy.—At necropsy, following death from intercurrent lobar pneumonia, the cecum, and ascending and transverse colon showed amebic ulceration, which was quite advanced about the hepatic flexure.

In addition to latency, the symptoms of this infection may be completely masked, and mistakes in diagnosis are, no doubt, frequent when the disease is endemic.

The clinical manifestations of several diseases may mask those of a latent or mild amebic infection. The scope of this paper will not allow a full discussion of these, and the subject will be treated more thoroughly in a paper soon to appear on the complications and sequelæ of amebic infections. Perhaps the most frequent of these conditions, and those which are also likely to lead to mistakes, are chronic constipation and gastritis or appendicitis. The latter of these has already been discussed.[2] Gastric symptoms of more or less severity are particularly prevalent in the tropics, both with and without amebic infections of the colon; and

2. Bull. 18,. Bureau of Governnment Laboratories. THE JOURNAL A. M. A., April 8, 1905, p. 1098.

for this reason, particularly when severe, often completely obscure the less active disease when present.[3]

Numerous examples might be cited, showing the variety and prevalence of such conditions; but my object here is to call particular attention to it, without leaving the impression that every case of stomach trouble in the tropics masks an amebic infection of the colon.

Constipation is a very prevalent condition in the tropics, as it is in the United States, particularly among women; and, as might be inferred, may frequently mask amebic infection in the early stages, and in the latent and less active forms until irreparable damage may have been done to the colon.

I have under my care now a woman who has for years been a chronic sufferer from constipation. About five months ago she began to lose weight and other symptoms developed, suggesting probable amebiasis, which was confirmed by microscopic examination of the feces. During this time, the constipation had persisted, notwithstanding that blood and mucus were obtained with every specimen secured by salts, and diarrhea did not develop until about two weeks ago. Dysenteric stools quickly followed, and treatment, which is still being given, was instituted.

Such cases as this and those previously described are of frequent occurrence in practice in Manila and support the conclusion which I have already expressed, namely, that the presence of amebas in the stools should always be considered diagnostic, at least in so far as treatment is concerned. The fact that one occasionally

3. I now have in mind such a case in a very prominent man in Manila. He had for years been a sufferer from chronic gastritis, and after a few months' residence in the Philippine Islands the symptoms became more aggravated, and just as previously, he had periodic outbreaks of diarrhea, only that with the increase in the stomach symptoms, the diarrhea became much worse. At the end of six months he was confined to his bed, unable to retain food, and reduced almost to a skeleton, and the bowel evacuations had become dysenteric. An examination of the feces showed numerous amebas with blood and mucus. Under careful treatment, directed particularly to the amebic infection, he slowly improved and was eventually restored to his usual health.

sees a case similar to those mentioned above, in which clinical dysentery never appears, the patient never feels ill, and amebas eventually permanently disappear from the stools, is not a sufficiently strong argument against the conclusion given, until such time as definite data indicating the final outcome are available early in the infection.

Mild and Moderately Severe Cases.—These form by far the great majority of those seen in Manila at the present time. Formerly they occupied about the same place as that occupied now by latent ones, i. e., they were treated as simple diarrheas from other causes, and often the true nature of the infection was not recognized until the development of bloody mucus discharges, or more often the pathologic report called attention to it.

The symptomatology of this class of cases, as well as that of the more severe cases, is so well understood and has been so often described that I will condense that part of the paper into calling particular attention to the conclusion which we have come to in our work in Manila, that diphtheritis and other acute pathologic processes seen at postmortem in this disease are the result of other etiologic agents and are not a part of the true amebic infection.

The larger number of these cases develop from the latent ones already described, just as the majority of the more severe ones usually arise from this type. It is impossible to say just what proportion of them develop as such primarily or follow a more or less definite latent period; clinically, the time of onset is usually dated from the appearance of diarrhea. There may be prodromal manifestations before the onset of diarrhea or dysentery in cases in which amebas may not be found at the time, but here the prodromes are very like the manifestations of the latent type, viz., indefinite abdominal pain, generally attributed by the patient to "taking cold" and explained by not a few as being caused by sleeping with-

out an abdominal band on certain cool nights; tenderness on palpation along a part or all of the colon, "indigestion," headaches, usually of a dull cerebral type, a general feeling of depression, ill health and irritability of temper, and sometimes melancholic tendencies, with anemia and loss of weight.

In the majority of properly treated patients the disease clinically rarely passes from diarrhea, but sometimes here as well as in the larger number of untreated ones diarrhea is only preliminary to a more violent clinical picture. Many cases, however, even without treatment, never become dysenteric in the general acceptation of the term.

The course in uncomplicated cases is extremely chronic and the outcome rarely recovery, being most commonly the development of "sprue" or chronic gastroenteritis giving other clinical pictures; and the most frequent termination is death from intercurrent disease or complications. I am still in correspondence with a number of old Manila patients, now in the United States, in which the cases are of from four to six or more years' duration, and in which symptoms are still very much the same as when the patients left Manila.

Following a gradual onset from a period of known latency, the diarrhea is usually intermittent and more marked in the mornings, consisting of two, three or four soft, semi-fluid stools, without mucus or blood and passed without pain. This condition may last from one to several days, and is usually followed by a tendency to constipation. Succeeding outbreaks usually become more severe and may last for days, weeks or months, until the appearance of blood or mucus causes the patient to realize that he has dysentery, and it is at this stage that he most often appears for treatment. When the onset is more sudden, some blood and mucus are frequently noticed in the stools from the first; there may be some tenesmus and symptoms may continue for a few days, to be followed, as in the first case, by a period of

constipation. The subsequent course of the disease in the two cases may not be different, but usually the more acute the onset the more rapid development of more severe symptoms. It is certain that in not a few of these the sudden outbreak is not due to amebas, but to other causes. There are frequently the same extrinsic causes for these outbreaks as when they occur in subjects free from amebas, which is, of course, of frequent occurrence in the tropics, and, in addition to this, careful inquiry will often reveal that there were significant manifestations before the onset in the amebic cases, and it may even be observed when amebas were known to be present for some time prior to the outbreak.

Severe Cases.—The clinical aspects of this type of the disease are the best understood and carefully described, and need but a brief summary here. As is true of the class of cases just discussed, in by far the greater number of cases it develops from a previously existing latent or milder type.

To this class belong also the diphtheritic and gangrenous cases, which are always severe and are undoubtedly due to a concomitant or secondary infection with some other agent, which is also the cause of severe forms of other types.

The onset here, whether occurring in an apparently healthy subject or following an existing milder type, is usually quite sudden and is characterized by the phenomenon of an acute dysentery from other causes. There are frequent mucus bloody passages, with tenesmus, colic, thirst and perhaps some fever.

In this severe form, whether apparently primary or secondary to one of the milder types, the course is usually much shorter and death is frequent from toxemia, perforation of an ulcer or from exhaustion of the patient. There are cases in which postmortem examination may show excellent nutrition and a rotten intestine, with either extensive gangrene or diphtheritis. Even in these, however, not infrequently the severe symptoms

subside under treatment, and the case may continue as a more moderate one, or may be even mild in its symptoms, thus exemplifying the previous statement that the clinical types designated may frequently change from one to another even in the same patient.

Infection in Children.—Particular attention has been called to the disease in children by several writers.[4]

I have had twenty-one cases in children between the ages of 6 months and 10 years in private practice in the Philippine Islands, and one necropsy in a girl 3½ years old. When we consider the increased danger of infection which is present for children in the tropics, we must conclude that they present an increased natural immunity, a fact which is still further borne out by a study of cases in which infection does occur, for the disease is usually of a very mild type and is very amenable to treatment. In only two of my cases (in addition to one death) was the disease what could be called moderately severe from its clinical manifestations. The symptoms, in general, conform to the milder types in adults, and recovery is almost certain under proper treatment. I have seen children in whom there was undoubted active infection recover without treatment.

The aged, as in the case of children, seem to manifest a decided natural immunity; but, when once established, the disease in them is usually of more serious import than even in young adults. The symptoms are commonly of a severer nature, the course is more rapid, and the mortality higher, generally, as in other patients, due to complications or to intercurrent disease.

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4. Amberg, in 1901, carefully reported five cases from the Johns Hopkins Hospital, and reviewed the literature on the subject. Harris reported thirty-five cases, four of them in children under 10 years of age. Strong found amebas in the tuberculous ulcers of a 3-year-old child; Slaughter in liver abscesses of a 17-year-old boy; Kartulis in children of all ages except infancy; Pfeiffer in the stools of several children; Lamb in a 2-year-old child; Lutz in the stools of a little girl; Sonsino in the intestinal mucus of a child; Cahen in a girl 4 years old; Gneftos in the liver abscess of a 6-year-old girl. Oddo (1897) reported twelve cases of liver abscess following dysentery in children between the ages of 2 and 13.

One thing particularly noticeable both in children and in the aged, as well as in natives of the Philippine Islands, is the great relative infrequency of liver abscess. I have not seen a case of liver abscess in more than one thousand clinical cases and one hundred autopsies of natives of the Philippine Islands.

Analysis of Symptoms.—All varieties of facial aspect are seen, from a healthy one in some of the rapidly fatal cases to the more emaciated, anemic, yellow and even cachectic of some in the old long-standing ones. Usually for a long time the patient does not appear to be ill, and I have seen patients with the disease of more than two years' duration who had lost no time from the daily occupation.

In the early part of the disease the skin rarely shows any noticeable change, but in the old emaciated cases there is a general waste and a scrawny, dull, goose-flesh skin, often of a muddy color or even jaundiced. In this class of cases there is frequently an odor which is quite disagreeable and which is as characteristic as for any of the diseases in which its diagnostic value is emphasized. Perspiration is usually not very active, but cases are occasionally seen in which the night sweats equal those of tuberculosis. Edema, particularly of the feet, ankles and less frequently at the hands, and the face about the eyes, is often present, but is not necessarily an indication of Bright's disease. Albuminuria and casts may be present at times when these edemas are noticed; and involvement of the kidneys is frequently observed post-mortem, though in the majority of the cases terminating in recovery the proper functioning of the kidneys is restored, and there is no further trouble from this source. Bed sores are rarely seen, except in the most chronic types of old emaciated, anemic patients, shortly before death. Boils are frequent in the tropics during convalescence from any wasting disease, and in amebiasis they are not exceptional. Of rashes, urticaria is of quite frequent occurrence and often annoying in its persist-

ence. Quinin rashes, from absorption of this drug, are the most frequent and troublesome, often requiring a suspension or change of treatment. Enlargement of the superficial lymphatics without pain is common, particularly among natives; but this is so frequent an occurrence in health and other diseases that diagnostic importance can not be attached to it.

Digestive System: The organs of digestion bear the brunt of this disease, and it is here that diagnostic symptoms are most frequently observed. The appetite is most generally good, particularly so in the latent and mild cases during the early part of the disease. Later catarrhal conditions of the upper intestine, stomach and even esophagus are followed by variations in the appetite, due to such alterations. In the early disease, likewise, but little or no discomfort is felt from satisfying a normal desire for food, but later such action is often followed by an increased diarrhea and by a further disturbance of the already disordered upper digestive tract.

The tongue is in no sense a valuable interpreter of the conditions at the seat of the amebic lesions. It may be clean or coated with furs of various colors and types. It may be large or swollen, showing the marks of the teeth along its edges, or it may be red and pointed. In very old chronic cases, in which the clinical picture is that of sprue, the tongue is one of the valuable indicators and here often shows small ulcers along its sides and under the tip. Glossitis, with superficial ulcers and hyperemia of the mucous membranes (sprue), is not uncommon, and when present causes a dryness and burning sensation, which is very annoying. In the same class of cases, too, the frequent lesions of the esophagus cause a burning pain along this viscus, which is aggravated by acids or solid food. Thirst is usually increased and often markedly so when the clinical symptoms are quite active, due, no doubt, to the loss of body fluids through the ulcerated bowel.

Symptoms referable to the stomach depend, for the

most part, on various stages of catarrh of this organ and do not differ from symptoms of similar conditions due to other causes. In the early part of the disease, the stomach most frequently remains in good condition, but in the later stages, and sometimes quite early, its symptoms may be very annoying. Nausea is frequent, but vomiting rare at any stage. Both these conditions are aggravated and frequently are direct sequences to treatment by enemas. Symptoms of hyperacidity, with beefy-red tongue and epigastric pain (heart-burn), are encountered from time to time in all classes of cases; but a fermentative condition, with gas, a large, coated, flabby tongue, nausea and loss of appetite, are more common conditions.

The small intestine may be normal, but sometimes in the more chronic cases it shows a general catarrhal condition, which manifests itself by the usual symptoms of enteritis of other etiology. True amebic ulceration occasionally extends for from 2 to 10 cm. into the ileum, and in one case a perforation of an ulcer above the valve occurred, and the symptoms brought about by it closely resembled those seen in severe infection of the cecum.

The Large Intestine and Feces: The bloody-flux interpretation of the word dysentery must be abandoned in this disease, or, perhaps, a better solution would be to change our nomenclature so as to avoid calling it dysentery at all. It is true that diarrheic, or even dysenteric, stools are present at some time during the course of the disease in the majority of cases which proceed to a fatal termination; but even here this is not always so, and true dysenteric stools are not the rule in patients in whom treatment has been instituted early and properly administered.

There are numerous examples in literature of patients who have died of the disease in whom during life there was slight or no clinical dysentery. Such cases have been reported by Councilman and Lafleur, Osler, Dock,

Strong and Musgrave and many others; and we (Mr. Clegg) have emphasized it in a recent paper.

In this paper I have already cited cases, and to them could be added at the present time a considerable number in which there was no diarrhea or dysentery at any period during the course of the disease, and yet death occurred from perforation of an ulcer or from intercurrent disease. Further, within the past year, in addition to a case already mentioned, I have performed the necropsy on the body of a patient who had been treated for more than six months for constipation, in whom advanced amebic ulceration of the cecum and ascending colon was found after death, resulting from perforation of a liver abscess. Such cases, of course, are not the rule, but they are sufficiently numerous to be of importance and are emphasized particularly for the purpose of demonstrating that, as in the case of many other infections, experience broadens our conception of the clinical picture.

With this data, I am prepared to state that in this disease there may be any stage between constipation and severe clinical dysentery, or alternations between these two conditions may be present throughout the course of the disease; and it is in this variation that we secure data for the arbitrary clinical division of the cases.

From what has been said it is seen that this clinical division is not necessarily borne out by the pathologic picture, and, therefore, it must not be inferred that the disease is of necessity mild because of the absence of a severe diarrhea.

In the great majority of cases, after a more or less prolonged incubation or period of latency, alternating periods of diarrhea and constipation develop, and usually the diarrhea becomes more severe with each return and persists longer, the constipation becoming less marked until finally formed feces are no longer passed. The diarrhea is usually more pronounced in the morning and after meals. In long-standing cases, the patient

complains that the food passes through unchanged as soon as eaten.

There is nothing characteristic in the macroscopic appearance of the feces. Their consistency, amount, color, etc., may vary between the widest limits. In the early stage of the disease they are frequently formed and otherwise normal, and the surface may or may not show coatings of mucus sometimes streaked with blood. The morning specimens are usually the first to have a diarrheic appearance and are often copious and fermenting. When the infection is more advanced, the feces may take on the appearance of those due to chronic catarrh—fluid, with mucus and particles of undigested food. On the other hand, frequent large, light gray fluid or granular, foul-smelling evacuations, with mucus, and with or without fresh or old blood, and sometimes masses of tissue and occasionally casts of the mucosa, may persist for weeks or months. Again, particularly when the infection is low in the colon and rectum and there is some severe secondary infection, the stools may resemble those of acute dysentery in character and symptoms produced. The odor of the feces in many cases is particularly offensive and all but characteristic, so much so that diagnostic importance may be attached to it. The next most important point of diagnostic value obtained from a macroscopic examination is the indication of the location of the infection by the character of the blood, when such is present.

Amebic infections can be diagnosed with certainty only by microscopic examination of the feces or other material, and by this method also other valuable data may be obtained.

The best method of securing a specimen and the manner of procedure for microscopic examination have been described in *Bulletin* No. 18, Bureau of Government Laboratories, and some additional points are mentioned under the heading of diagnosis in this paper.

The presence of motile amebas should be considered

diagnostic, at least in the tropics. The difference in size and numbers, the presence or absence of enclosed blood cells, and other described points of differentiation, I believe to be fallacious, as pointed out in a previous publication.

Many other parasites and substances of more or less importance are often found associated with amebas. Among animal parasites are the *Trichomonidæ, Cercomonidæ, Megastoma entericum, Embryo strongyloides,* ova of uncinaria, *Trichuris, Tænia, Oxyuris,* and others, either singly or in various combinations. At least some of these have a part in the production of the symptoms and must be reckoned with in treatment. Of other substances present may be mentioned leucocytes, red blood cells, pus, epithelial and other cellular elements. Various crystals are often present, but with one or two exceptions are of no diagnostic importance. Many other substances may be found, but as they have been so repeatedly discussed by others and are of such slight importance to the subject in hand they will be omitted.

Circulatory System: The circulatory system in this disease shows essentially the changes of secondary anemia. The pulse is usually of good quality, except in the later stages or in the presence of complications, when it takes on a type due to such involvements. Early in this disease the blood shows little or no change, the red cells being normal in numbers and free from abnormal elements, the leucocyte count is normal, the relative proportion of the cells is not disturbed, and the hemoglobin estimate is also normal. As an uncomplicated case progresses, the red cells begin to show changes due to anemia, and in the later stages the irregularity in their size and shape may be quite marked, and the count may show great reduction, notwithstanding the loss of fluid from diarrhea. The leucocytes under like conditions show some disturbances in relation of varieties, usually an increase in polynuclears and eosinophiles, but these changes are never such as to be of diagnostic

value. Hemoglobin decreases with a reduction in the number of red blood cells. The spleen is not enlarged, except in some severe cases complicated by or associated with other infections.

Temperature: Fever is most often absent throughout the course of the uncomplicated disease. It may be present in a moderate degree, when it is usually of an intermittent type, highest in the afternoons. In acute exacerbations from any cause, and when there is an intense secondary involvement, particularly diphtheritis, it may be an important factor. Only recently I was for some weeks very much puzzled by an intermittent temperature, reaching its maximum of from 38 to 39° C. about 10 o'clock a. m. daily, in an amebic patient, until other symptoms proved the presence of an intercurrent syphilis. It is frequently found, but by no means constantly so, in liver abscesses. Here, if the abscess is also the seat of bacteria in considerable numbers, the septic temperature may closely resemble that of a malarial infection, endocarditis or almost anything else, of either the intermittent or the remittent type. On the other hand, one occasionally finds a large liver abscess without fever at any time. As the disease becomes more advanced, it is quite common for patients to exhibit subnormal temperatures, particularly during the forenoons, for days, weeks or months in succession.

Nervous System: This probably does not suffer much as a direct consequence of amebic infections, but of this I am not at all sure. There are many cases of neuritis, neuralgia, etc., which are so closely connected with the disease that until we are more fully acquainted with the exact method of the action of amebas in other parts of the body, our opinion can only be based on supposition.

Pain: The subject of pain in general, however, may be conveniently discussed here. Its variety and intensity in this affection is very great. It is partly a direct consequence of lesions and partly the result of more remote and sometimes unexplainable causes.

Tenesmus is more often an indication of complications or severe secondary involvement than of amebic infection. It is never present in the latent forms and is usually absent or very slight in those of moderate severity; but during acute exacerbations of either of these, and particularly when diphtheritis or other secondary infection, including that of *B. dysenteriæ Shiga,* is present, it may be very severe. It is much less severe or more likely absent when the lesions of whatever type are in the cecum or upper part of the colon.

Colicky pains are not infrequently seen, and even severe acute intestinal colic sometimes supervenes, especially when there is marked catarrh of the small intestine.

Dull, aching, somewhat indefinite abdominal pain is one of the most frequent prodromal symptoms, and quite frequently it is persistent during the disease. Sometimes it is so severe and constant that rest is impossible for days or weeks at a time. Though most usually complained of as being of maximum intensity along the course of the colon, as general careful palpation will show, not unusually it is found only in the region of the cecum and is sometimes complained of in the muscles of the back. Such pain may be due to the processes going on in the bowel, and, again, as demonstrated by postmortem examination, it may be the only indication during life of the most extensive serous inflammations and adhesions. These pains are often most active in the night, even in the mildest cases of infection, and may interfere seriously with the patient's rest.

Pains described by patients as "heart burn in the abdomen" may be general or more frequently local. When active lesions are low in the sigmoid and rectum, these and what are described as burning pains are frequent. The latter may be intense about the rectum, and may sometimes extend down the backs of the thighs and even to the calves of the legs. Old sciaticas are often "fired up" under these circumstances, and the begin-

ning of sciatica is associated with such cases often enough to be suggestive.

Pains simulating those in appendicitis have been more fully discussed in Part 2 of *Bulletin* No. 18, Bureau of Government Laboratories, and in the JOURNAL A. M. A., April 8, 1904. They are probably the most important with which we have to deal, because their true interpretation is so vital to the patient and because they are of such general occurrence in all varieties of amebic infection, from the latent to the gangrenous, with or without the presence of amebic or other forms of appendicitis.

Neuralgias, myalgias and arthralgias are met with too frequently to allow them always to be considered accidental associations. Persistent, dull headaches, particularly of the back of the head and neck, are also not uncommon. The genitourinary and respiratory systems and the organs of special sense rarely contain lesions which produce symptoms of any importance in the uncomplicated disease. The same is true of the joints and the osseous system, though complications may involve any of these structures.

DIAGNOSIS.

There are no classical symptoms in the disease, and hence an absolute diagnosis can be made only by microscopic examination of the feces.

In remote areas where the infection is endemic and where microscopic facilities are not available, one would be justified in making a diagnosis for purposes of treatment from clinical manifestations alone, but where laboratories are accessible this should never be done.

If one remembers the multiform clinical pictures which have already been discussed and watches the case for some time, a diagnosis of amebic infection may reasonably be inferred, but it must be borne in mind that the clinical picture does not in general differ materially from that often seen in diseases with an en-

tirely different etiology, and, further, that there is not a single symptom or group of symptoms which is confined to this disease alone.

The following are the most important clinical manifestations in a question of diagnosis:

1. The bowel evacuations, particularly their odor, and the presence or absence of blood. Their consistency, quantity, frequency and the presence or absence of mucus, are much less important.

2. Abdominal soreness, which is increased on pressure and extends particularly along the colon, is most common and, taken singly, is one of the most valuable symptoms. Its diagnostic importance is greatest when of maximum intensity over the cecum and ascending colon.

3. So-called "indigestion" headache, general lassitude, with nausea or pain below the stomach after eating, etc., is quite common, but is also prevalent at other times, so that but little importance must be attached to it alone.

4. Loss of weight, especially in the presence of a good appetite, is quite important and is the best guide to the progress being made by the infection.

As already stated, neither one nor all of these symptoms taken together are sufficient for an absolute diagnosis; but when taken together in cases where careful palpation reveals a thickened, tender colon in places where it may be felt, they make the nearest approach to a sure diagnosis possible without microscopic examination of the feces.

The question as to whether the presence of amebas in the feces is always absolutely diagnostic of an infection of the colon has already been discussed. It may be that such is not always the case, but I believe that it is so nearly so that such an occurrence, at least in the tropics, should be considered diagnostic, at any rate for purposes of treatment. Such a conclusion is all the more justifiable when we consider the great certainty of good

results in treatment instituted early, the long incubation period or latency which severe cases may show, the inability ever to establish a more certain diagnosis in those cases of light infection which terminate in recovery and, finally, above all, *the great reduction of the danger of liver abscesses by instituting early treatment.* It will be remembered that, according to statistics from many places, including Manila, over 20 per cent. of untreated patients or those not treated by enemas have developed liver abscesses, and that in a very large number of patients treated by my colleague and myself in private practice during the last few years, along lines laid down in *Bulletin* No. 18, there have not been more than two cases of liver abscess which developed after treatment was instituted. Inasmuch, then, as a correct diagnosis can be made only by finding amebas in the intestinal contents, and as their presence here, at least for purposes of treatment, are to be considered diagnostic of infection, regardless of clinical symptoms, the best method of determining their presence or absence should be part of our subject.

This is not always an easy matter. When there is active clinical dysentery, a microscopic examination of one of the passages will usually reveal amebas, but even here single or even several examinations will often yield negative results. The specimen for examination should, when practicable, be one obtained by some hydragogue cathartic, because the infected area frequently includes only a portion of the colon, and by this means the specimen is more certain to contain feces from the entire track.

For the same reasons, the method of extracting a specimen through a speculum can be of maximum value only where the lesions are in the lower bowel. For obvious reasons castor oil is not a satisfactory cathartic for this purpose, and specimens obtained by enemas are likewise unsatisfactory.

The specimen should be as fresh as possible when

examined, for, while amebas will usually remain motile for several hours and sometimes for days, in many instances they lose their motility in a very short time. In Manila, a warm stage will never be found necessary, and a diagnosis had best not be made from any but motile organisms.

Usually no difficulty will be experienced in differentiating amebiasis from other diseases, but when other troubles exist as complications or associated diseases, which is of very frequent occurrence, the solution is often not so simple. Suffice it to say here that in practically every instance in which such complications or associations do exist they are rarely of a nature which offers contraindication to the institution of the usual treatment of amebiasis, and, therefore, whether or not the nature of the complicating trouble is determined, treatment of the amebic infection should be prosecuted.

PROGNOSIS.

The prognosis in this infection should take several points into consideration, and the evidence in each individual case should be carefully weighed before an expression of opinion is justifiable.

Fortunately, in Manila, owing to the good results of treatment, the physician is rarely called on to say very much; but in the more prolonged and persistent cases prognosis is eagerly sought by the patient and his friends. In general, under proper treatment recovery is the rule in young, well-nourished adults, in whom the disease is not of too long duration.

The principal determining factors in giving such prognosis are the manner of treatment, age, nationality, general condition of the patient and duration of the disease at the time treatment is instituted, reaction to treatment, the presence of complications and associated diseases, and, finally, the location of the amebic lesions.[5]

5. In my last 100 completed cases treated in private practice including all types and stages of the disease, 96 patients have permanently recovered without leaving the Philippine Islands. There has been one death and three have returned to the United States.

It must be remembered that in a certain percentage of cases, particularly in children and natives, the patients recover from the disease without any treatment whatever. On the other hand, one occasionally sees a patient in whom the disease is progressive from the first, and death is not apparently delayed by any form of treatment.

The disease is generally milder in children and in natives of the tropics, and its course is more often shorter and its mortality higher among the aged. Alcoholics apparently are less frequently infected, but when once the disease is established the gravity of the prognosis is increased. Previous good health and good general physical condition are favorable factors. The shorter the duration of the disease at the time treatment is instituted and the greater the tolerance for enemas the more favorable the prognosis.

The presence of complications or associated troubles, such as liver abscess, severe hemorrhoids, fistula or fissure in ano, and many others less frequent, materially decrease the chances of ultimate recovery. Probably most important of all, however, is the location of the lesions. As a rule the higher up the lesions, the greater the mortality and the less active the clinical dysentery. Severe infections of the cecum, unless treated early and carefully, are always serious.

CONCLUSION.

In conclusion, I wish to emphasize the fact that intestinal amebiasis (amebic dysentery) manifests itself in a much broader and more comprehensive clinical picture than is generally allotted to it.

Waiting for bloody mucus stools to appear before making a diagnosis and instituting treatment is responsible for a large percentage of the present mortality from the disease in Manila. Such stools sometimes appear early in the disease, more usually after considerable damage has been done, and occasionally are never seen before a fatal termination or recovery.

Suppose, for example, that by treating every patient in whom motile amebas are found, as recommended in this paper, we do occasionally treat a person who would have recovered without treatment, or possibly would never have had an active lesion, are we not justified, when we consider that by such procedure established early, without waiting for clinical dysentery, we increase many fold the chances of recovery of all patients?

THE PATHOLOGY OF INTESTINAL AMEBIASIS.

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In former papers, one of us (Musgrave) has dealt with the subjects of the cultivation of amebas, and the etiology, diagnosis, prognosis and treatment of intestinal amebiasis. To complete the series, there remained, then, the pathology, complications and sequelæ, and to the pathology of the intestinal amebic disease the following remarks will be limited.

It may be well to state at the outset that we can see no valid reason for departing from the nomenclature of Lösch. He described a *pathogenic* ameba from a diseased intestine and called it *Amœba coli.* Why this term should be applied to a supposititious non-pathogenic organism is difficult to say. We shall, in referring to the cause of intestinal amebiasis, use the name introduced by Lösch.

Among the many articles in the literature of amebiasis, there are but few which are of special value from the pathologic side. Chief among these are those of Councilman and Lafleur,[1] Harris,[2] Howard,[3] and

1. Johns Hopkins Hosp. Reports, 1891, vol. ii, 395.
2. Amer. Jour. Med. Sc., 1898, vol. cxv, 384.
3. Buck's Reference Handbook, 1900.

Rogers.[4] Taken together, these works give a very complete picture of the disease as we have seen it.

The material has been obtained from various sources, among which have been the First Reserve Hospital (the records of Strong and Musgrave), Bilibid Prison and the Civil Hospital, all in Manila. Other material has been obtained from the private practices of Drs. McDill and Musgrave, also in Manila.

METHODS.

Bits of tissue from autopsies were fixed in Zenker's solution, in absolute alcohol, Flemming's solution, and Kaiserling, and ultimately imbedded in paraffin.

Sections from alcohol tissues were stained by Mallory's thionin and oxalic method, those from Flemming's solution in safranin and safranin-picro-indigo-carmin, those from Zenker's in Magenta-picro-indigo-carmin (Borrel), Gentian-violet-picro-indigo-carmin, eosin-methylene-blue, eosin and toluidin blue, hematoxylin and eosin, hematoxylin and picro-fuchsin (Van Gieson), chlorid of iron hematoxylin (Mallory), and Heidenhain's iron hematoxylin.

After some preliminary staining it was evident that for simple diagnosis of amebas from alcohol tissues, the eosin-toluidin-blue and thionin-oxalic-acid methods were satisfactory in the order given; for others, sublimate or chrome tissues, hematoxylin and eosin were most useful. It was evident, however, that for careful examination and cytologic study the best results could be obtained with Heidenhain's iron hematoxylin and Borrel's stain, or in the case of Flemming's solution sections with safranin-picro-indigo-carmin. Borrel's method may be modified by using gentian violet in the place of magenta with excellent results.

Borrel's staining gives most brilliant results in sublimate tissues producing very clear distinct pictures and only surpassed in clearness and delicacy by Heidenhain's iron hematoxylin. Both of these stains

4. Brit. Med. Journ., 1903, vol. i, 1315.

have the additional advantage of showing the bacteria when differentiation is properly carried out.

Hematoxylin and eosin is a very satisfactory routine method for demonstrating the amebas although the contrasts are not so distinct and the finer elements can not be so well demonstrated.

Harris' method, when applied to sections of the intestine, gives a considerable contrast between the amebas and other cells. By its use the organisms are easily found with the lower powers of the microscope.

Kaiserling tissues respond best to hematoxylin and eosin, but are of little comparative value for detail, and have been used almost exclusively to demonstrate the lesions in a gross microscopic way. From such tissues, serial sections have been made of various types of lesions and their form and extent studied in that way.

GROSS LESIONS.

Many writers say that the macroscopic lesions of intestinal amebiasis are pathognomonic. While in certain cases—perhaps in the majority—this is true, there are others in which the picture may be very deceptive. We have seen cases from the appearance of which at autopsy we could not say definitely whether or not we were dealing with amebiasis, tuberculosis or some other ulcerative condition. We have seen some cases, few to be sure, in which the majority of the ulcers were not of the classical undermined type, in which the undermining was either incipient or healing was in progress. A truly pathognomonic picture, however, is presented when the mucous membrane shows all the types of lesions, and this is not uncommon, and in which the walls of the gut are thickened and edematous.

The various lesions may not be sharply distinguished, for the process is a progressive one, and one type shades into another very gradually, so that it is for purposes of

Fig. 1.—Thin-walled gut, with shallow ulcers, some slightly undermined, others punched out.

Fig. 2.—Both edges held ready for suturing.

Fig. 3.—Colon. A moderately thickened gut with various types of ulcers.

convenience in description that we shall apply epithets to arbitrary stages of the gross process.

1. *Preulcerative Lesions.*—These are the "small raised

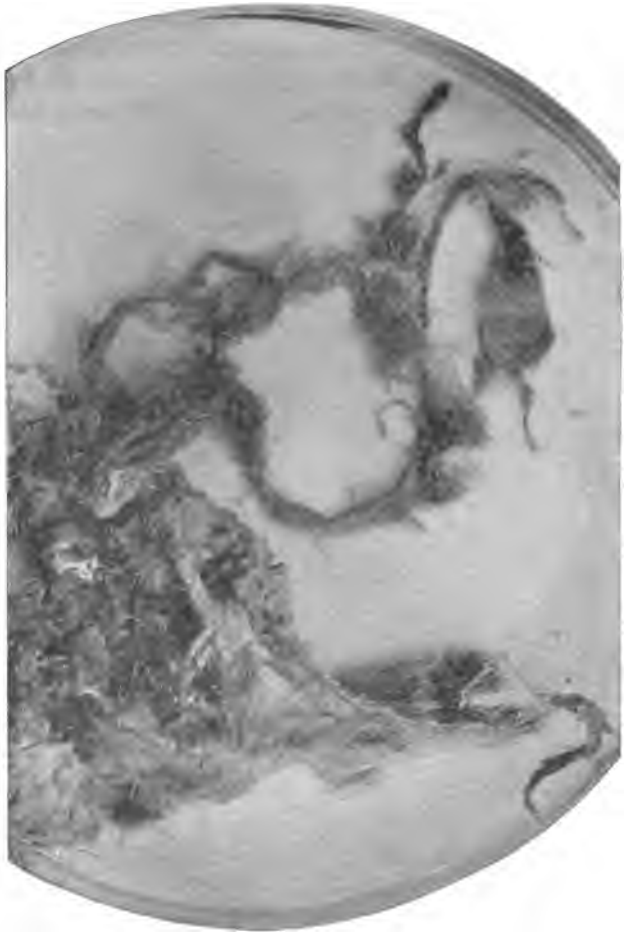

Fig. 4.—Cecum. Marked degree of disorganization of the bowel with shreds of muscularis and submucosa. Perforation.

dots" of Rogers. They vary in size from 0.5 to 2.0 mm. in diameter and are intensely congested. As a matter of fact, when studied macroscopically, they are seen to

be composed of one or more capillary hemorrhages into the intraglandular tissue. Usually associated with this condition is one of erosion of the superficial layers of the mucous membrane. These erosions, however, may be encountered in the absence of any marked congestion, although a moderate injection, at least, is the rule. With both of these processes there is little of the marked thickening of the submucosa that is so constantly seen

Fig. 5.—Rectum. Extensive ulceration and diphtheritis. Thick-walled gut.

in the more active ulcerative stages of the disease. These early lesions may be seen in any portion of the affected gut. By using the sigmoidoscope we have demonstrated them low down in the rectum within a couple of inches of the anus. They are most frequently encountered and are most numerous in the more acute cases, but may be seen also in quite chronic ones.

2. Ulceration.—A.—Type of Harris: These lesions,

though rarer than the classic type, are nevertheless not uncommon. They are possibly the result of the process of erosion mentioned above and are primarily confined entirely to the mucous membrane. As Harris says,

Fig. 6.—Various stages of ulceration.

they "generally reach into the submucosa and rarely to the circular muscle, but never deeper." They probably commence as a very circumscribed erosion and spread laterally as rapidly as they do downward. Macroscopi-

Fig. 7.—Colon. Extensive distribution of punched-out ulcers; some slightly undermined.

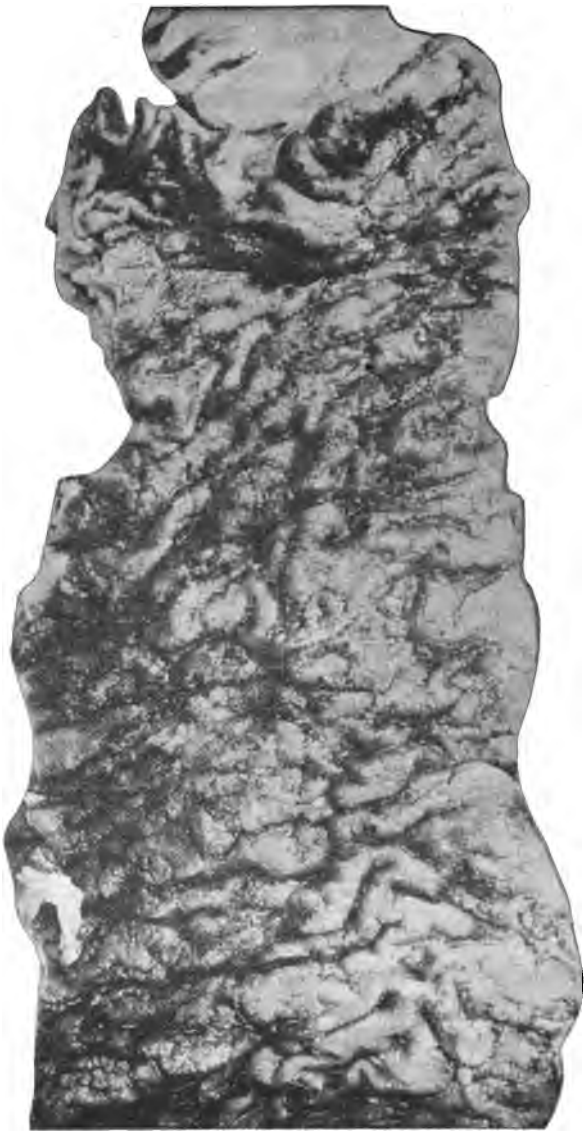

Fig. 8.—Colon. Thickened bowel with some large ulcers and some very early ones.

cally, the edges are abrupt, sometimes giving the ulcer a "punched-out" appearance. They are round or oval in form and their edges are usually thickened and marked by intense congestion. Their bases are comparatively clean, grayish and edematous. They are often situated on the apices of intestinal folds and have a tendency to increase in the direction of the short axis of the bowel. This type of ulcer has a general distribu-

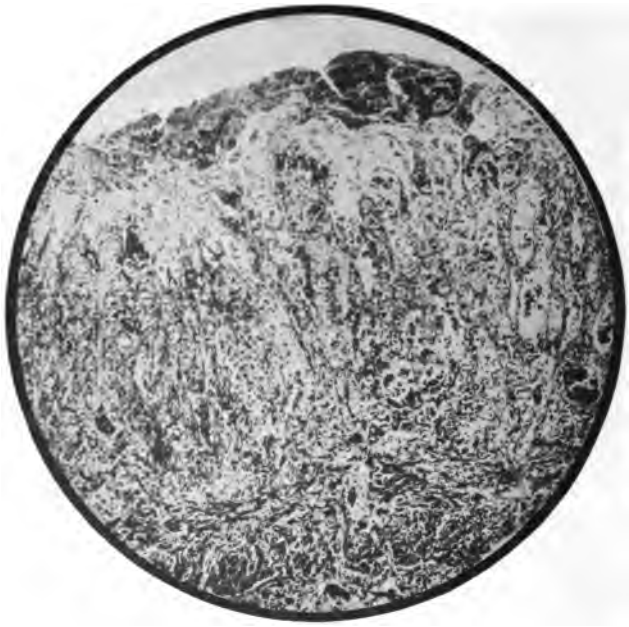

Fig. 12.—Early intestinal lesion. Shows superficial necrosis, glandular distortion, and round-cell infiltration. Borrel's stain. Zeiss obj. AA, oc. comp. 4, bellows at 30 cm.

tion and may be encountered in any part of the bowel. It is less frequently seen in the more advanced and very chronic stages. The fact that it is most common in those bowels that show the preulceration lesion speaks for its being intermediate between the very early petechial lesions and the undermined ulcer. This is the type most common in the ileum.

B.—Classic or Undermined Ulcers: These are seen

in an early stage as minute yellowish or grayish spots in the mucosa of the bowel, frequently at the centers of the petechiæ spoken of as the preulcerative stage of the disease, and are usually surrounded by a zone of congestion more or less well marked as the case may be. These spots represent the mouths, filled with necrotic material, of passages leading to larger or smaller cavities in the submucosa, which are also filled with the same material.

Fig. 13.—Early lesion. Extending necrosis, destruction of glandular epithelium, invasion of amebas, and round-cell infiltration. Borrel's stain. Zeiss obj. AA, comp. oc. 4, bellows at 30 cm.

As the process extends, the pocket in the submucosa is enlarged parallel with the surface in all directions, and, although the necrobiosis eventually involves all the coats of the bowel, the muscular layers and the mucous membranes suffer less rapidly, so that there results an ulcer with its base on the circular muscle and with overhanging edges of mucous membrane. Such ulcers may be of sizes varying from that of a pinhead up to that of

the palm of the hand, and may occur in any part of the large intestine and even in the lower part of the ileum, though in the latter they are smaller.

During the process of ulceration, the submucosa becomes generally thickened and edematous, as may also the muscular layers and the peritoneal coats.

During extension, such ulcers may coalesce beneath or on the surface, and it is no rare thing to find even

Fig. 14.—Submucosa in an early lesion. Borrell's stain. Zeiss obj. AA, comp. oc. 4, bellows at 30 cm.

small submucous pouches communicating with each other by small tunnels, while the mucous membrane may show no more than a catarrhal condition.

In many of the larger lesions, the circular muscle fibers are exposed, forming the base of an ulcer, and shreds of this may be seen nearly separated from the rest, and these shreds may be removed by gentle scraping. In still more extensive cases the muscular layer

may become necrosed or even perforated, and the ulcer may then be bounded externally by the peritoneum or omentum.

There are, perhaps, few diseases in which the omentum plays so important a protective part as in the one under discussion. Very early in the ulcerative stages this membrane may be found plastered on the peritoneal

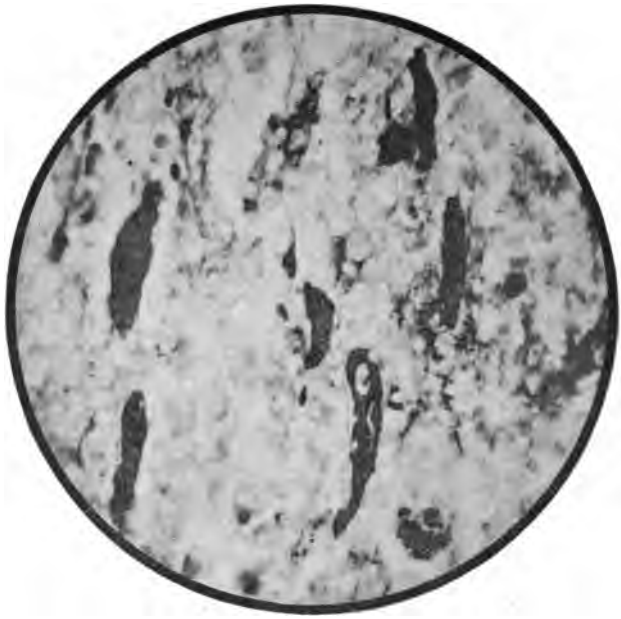

Fig. 15.—Thrombosis of blood vessels of the mucous membrane of the colon. Borrel's stain. Zeiss obj. DD, comp. oc. 4, bellows at 50 cm.

surface of the gut in preparation for the accidents that may follow.

Because of this function of the omentum, localized suppurations are common. Ulcers may also perforate into the subperitoneum at almost any point, and the abscess usually remains circumscribed or may furrow widely. In one case of this class, a furrowing abscess had perforated into the retroperitoneum in the cecal re-

gion and had extended upward and perforated into the right pleural cavity.

3. Healing.—As healing takes place, the mucous membrane gradually extends from the margins, so that in the early stages the ulcer seems to be lined with epithelium, except on its base. In the case of very small ulcers there may be complete repair, in other more advanced cases there is considerable formation of scar

Fig. 16.—Amebas in the muscularis mucosa. The section is the same as that shown in Fig. 13. x 500.

tissue which may lead to contractions. This we have not seen. The commonest outcome in cases of long duration, especially in those not treated systematically and continuously, is the establishment of a chronic catarrhal condition, with subsequent atrophy—a condition of chronic atrophic enteritis. This is recognized in various parts of the world as sprue or psilosis. It is not a result of amebiasis only, although it may be so in imperfectly treated cases. The gross features of the bowel in such a

condition are thinness, absence of normal folds, atrophy of the mucous membrane and increased length. Combined with this atrophic condition may be one of localized hypertrophy, resulting in the formation of more or less well developed polypi.

EPITOME OF THE GROSS APPEARANCES.

In a general way, the process studied is as follows: In the early stages of the disease there occurs a catarrhal

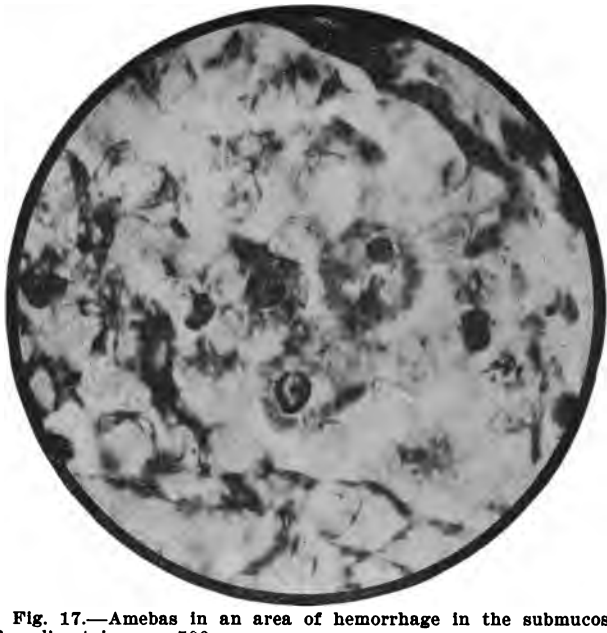

Fig. 17.—Amebas in an area of hemorrhage in the submucosa. Borrel's stain. x 500.

condition of the mucous membrane, with hypertrophy and cystic and mucoid degeneration. At various points, from the lower part of the ileum to the lower part of the rectum, small raised hemorrhagic spots occur, which later lose their mucous coverings and resemble erosions, and later still ulcerate. If abscesses have formed in the submucosa, they rupture into the bowel and form the early stage of undermined ulcers. The ulcers resulting from simple erosions are not, as a rule at least, of the

undermined type, but they may become so. Undermined ulcers are usually, while the cause persists, progressive.

When secondary infections occur, the processes of the disease may be modified by diffuse congestion, hemorrhage, diphtheritis or gangrene. Perforations may occur in the course of the ulcerative stages of the disease, with resulting localized or general peritonitis, retroperitoneal abscess, etc.

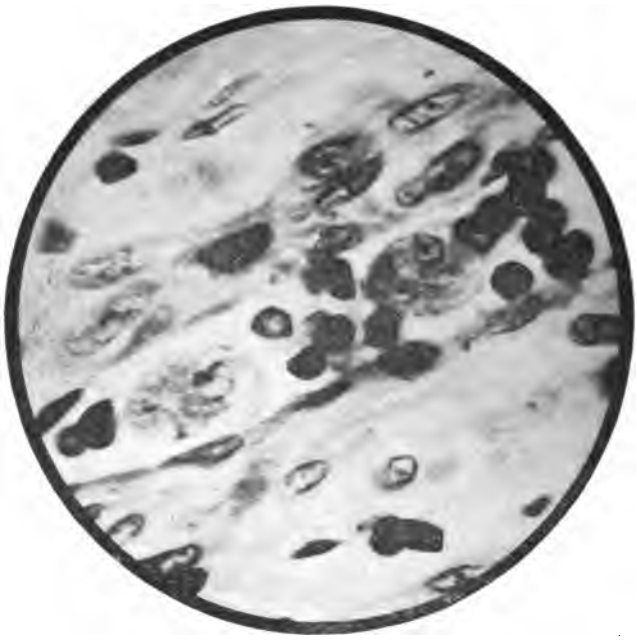

Fig. 18.—Amebas in a blood vessel. x 500. Heidenhain's iron hematoxylin.

The healing of small lesions may occur with complete repair, or of large lesions with the formation of scar tissue and with subsequent contractions. Peritonitis may result in the formation of adhesions. Complete cure may be the eventual outcome, or a condition of chronic atrophic enteritis or chronic catarrhal enteritis may result.

Generally, and probably always in active cases, the

intestine is thickened. This increase may be due to edema of all the layers, but chiefly of the submucosa. It may also be due to the presence of the abscesses and sinuses which are so common in that layer. In very severe cases the subperitoneal coat may be very much thickened, mostly from edema. The mucous membrane between the ulcers in uncomplicated cases usually appears normal.

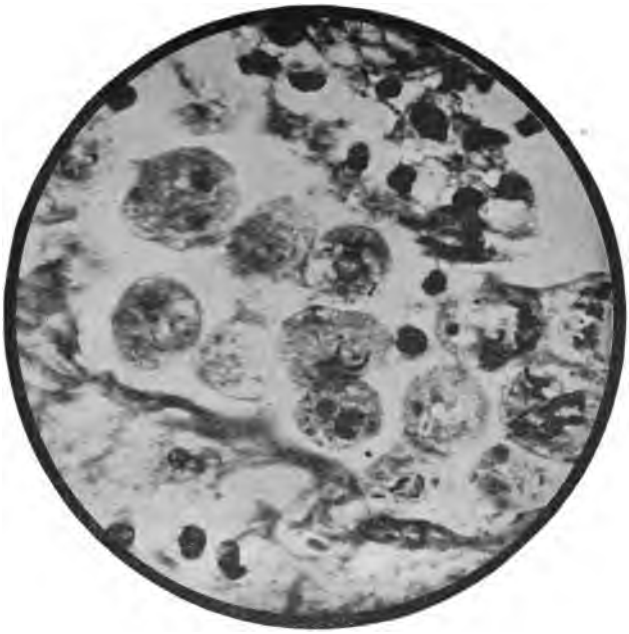

Fig. 19.—Amebas in a blood vessel. Borrel's stain. x 500.

DISTRIBUTION OF THE LESIONS.

There seems to be only a partial unanimity regarding the extent and localization of the lesions in the disease. To take recent remarks on the subject, Futcher[5] says that the rectum in a majority of cases is uninvolved or is so only to a slight extent. Harris[2] remarks that in fully half the cases the lesions do not extend above the

5. The Journal A. M. A., Aug. 22, 1903, p. 480.

beginning of the transverse colon, and Rogers[4] writes that almost invariably the lesions are more marked in the cecum and ascending colon and frequently are limited to these areas.

In considering the presence of lesions above the ileocecal valve, Futcher says that in two of 119 cases slight superficial ulceration was present in the last few centimeters of the small intestine. Rogers concludes that "the process never invades the ileum, which is contrary

Fig. 20.—Amebas in the lymph spaces of the submucosa. Borrel's stain. x 500.

to frequent results in other forms of dysentery." Many writers speak of the more or less frequent involvement of the appendix. Such observations taken from literature might be multiplied many times, but these serve to show how different are the results of careful and accurate observations based on studies carried out in different countries and even in different parts of the same country.

STATISTICS.

Our statistics are based on two series of cases, each of which comprises one hundred cases.

Series A is composed of cases in which the treatment was either unsystematic by enemas or none at all.

Series B is composed of cases treated by rectal injections.

SERIES A.

Entire large bowel involved (except extreme lower part of rectum)	87
Lesions confined to cecum and ascending colon	5
Lesions confined to transverse colon	1
Lesions confined to descending colon, sigmoid and rectum	0
Not recorded	7
	100
Appendix ulcerated (with large intestine)	6
Ileum ulcerated (with large intestine)	2

SERIES B.

Entire large bowel involved	72
Cecum and ascending colon	18
Descending colon, sigmoid and rectum	9
Transverse colon	1
	100
Appendix involved (with large intestine)	8
Ileum involved (with large intestine)	5

The variations shown in the two series, and those in literature as well perhaps, may be at least partly explained. The factors to be considered are the duration of the disease at the time of death, the kind of treatment, its duration and the stage of the disease in which the patient was when treatment was commenced.

If we take the Johns Hopkins Hospital series as an example, we may be reasonably sure that the majority, if not all, of these patients were treated by irrigations by rectum, as in our cases of Series B. A rational consequence of this might be that in many cases the lower lesions in the bowel had healed, and at autopsy only those that were inaccessible to treatment or which irrigations had not reached would be seen. This undoubtedly accounts, in part, for the variations manifested in our series, and this dissimilarity would undoubtedly be more prominent had a larger number been properly, consistently and persistently treated.

The duration of the disease at the time of death is

unquestionably an exceedingly important factor in untreated cases and in those in which irrigation has been neglected. It may be said that without treatment the greater the duration of the disease the more extensive is the distribution of the lesions.

For the reasons indicated and for other obvious ones, it may be said that the findings at necropsy can not be taken as a guide to the distribution of the lesions at any period save that immediately preceding death.

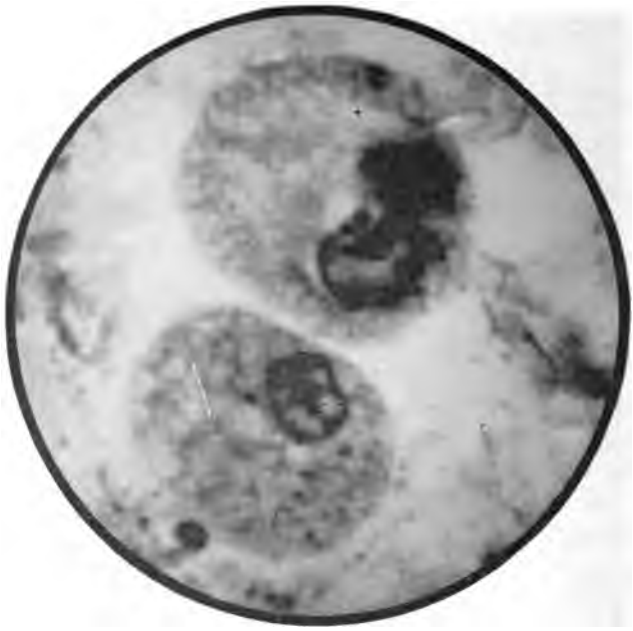

Fig. 21.—Amebas in tissues. Borrel's stain. x 1,400.

We have selected from our series twenty-five cases in which death occurred from intercurrent disease early in the amebic process, and find that among these there is an increased proportion of cases showing ulceration confined to a portion of the intestine and a coincident decrease in the number showing ulceration throughout the large gut.

Ulceration confined to the cecum and ascending colon.....	11
Ulceration confined to the descending colon, sigmoid and rectum	8
Ulceration throughout the bowel	6
	25

Lesions of the small intestine, in our experience, have always been confined to the lower ileum and have been the apparent result of direct extension from the cecum, which is usually severely ulcerated in these cases. We have had one case in which ulceration extended 32 cm.

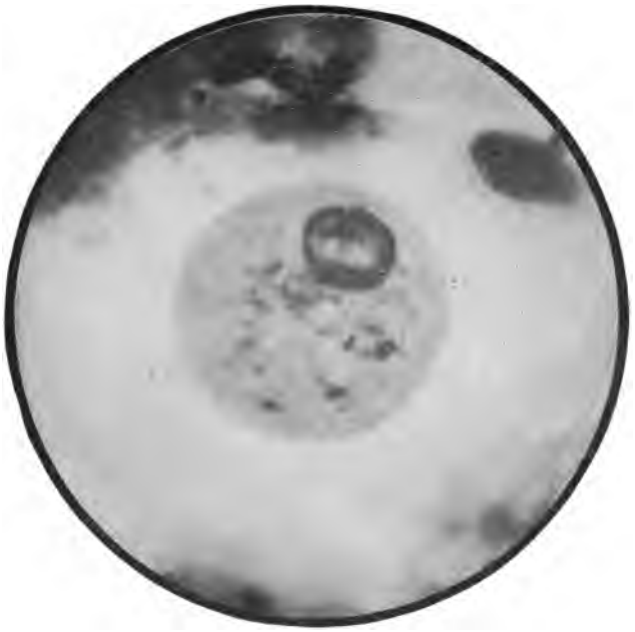

Fig. 22.—Amebas in tissues. Borrel's stain. x 1,400.

above the ileocecal valve, but ordinarily the lesions consist of one or a few ulcers immediately above, or within 5 c.c. of, Bauhin's valve. When, however, there is a diphtheritis of the cecum, the membranous exudate more often extends above the valve for a longer or shorter distance, but without ulceration. In such cases amebas have not been demonstrated, and consequently the cases have not been included in our statistics.

As in the small intestine, so in the appendix, only cases with distinct ulcerative processes, in which amebas were demonstrated, have been included in our statistics. In many necropsies, this organ was found clinically diseased from causes other than amebiasis and occasionally showed an acute process which could not be proved to be due to amebas. All such cases have been excluded from the tables.

Fig. 23.—Amebas in tissues. Borrel's stain. x 1,400.

HISTOLOGY.

In general it may be said that the mucous membrane between the ulcers is but little changed. In many places no changes from normal can be noted. In the immediate neighborhood of the lesions, however, there is a tendency to hypertrophy, with mucoid degeneration and even cyst formation. The latter is less common in the cases we have studied than in those reported by Councilman and Lafleur. The most common change in the mucosa is in the immediate vicinity of the lesions and

is shown by a tendency to more diffuse staining than is seen in normal epithelial cells; and whenever this, perhaps a sign of incipient coagulative necrosis, is seen, there is usually some distortion of the glands beneath the surface. Such changes are most frequently seen in the very early stages. In many cases, the cells lining the glands are separated from the basement membrane and lie singly or in clumps in the lumen. Under such

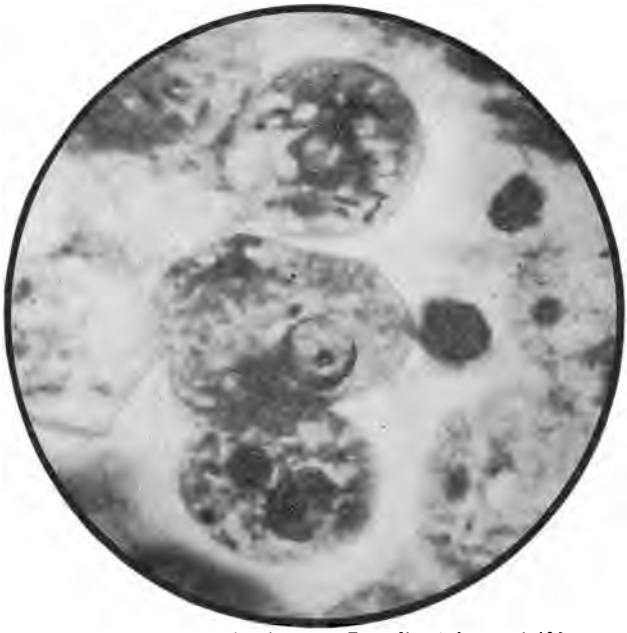

Fig. 24.—Amebas in tissues. Borrel's stain. x 1,400.

circumstances it is not uncommon to see amebas lying among the desquamated epithelial cells or forcing their way between such cells and the basement membrane.

The most marked feature of the early lesions is congestion, often combined with capillary hemorrhages which are most noticeable immediately beneath the mucosa. This congestion may extend even to the submucosa, in which layer there is also a certain degree of thickening due chiefly to edema. Together with con-

gestion, there is an increase of cellular elements of the lymphoid type in the interglandular tissue. The muscularis mucosa at this stage of the disease may show no changes or only a slight edema.

The most interesting feature of this early process lies in the distribution of the amebas. Not only may they be seen in the glands as described above, but they may also be present, sometimes in large numbers, in the in-

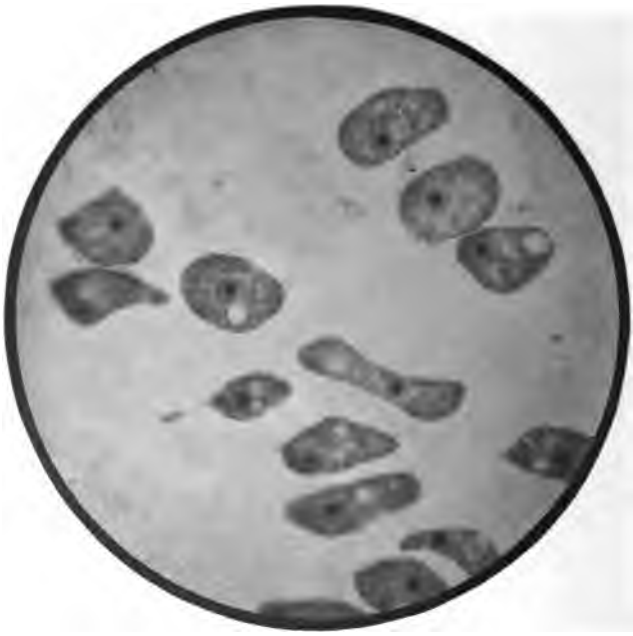

Fig. 25.—Amebas from a culture. Impression preparation. Borrel's stain. x 500.

terglandular tissues and blood vessels, in the muscularis mucosa and in the dilated veins of the submucosa, and this with changes scarcely perceptible to the naked eye or if only the low powers of the microscope are used. *In such lesions, bacteria are very few in number and often can not be found even after prolonged search, and none can be demonstrated in the amebus.* These show even in the blood vessels the peculiar rod-shaped or crys-

talline bodies that stain intensely with magenta and hematoxylin, the radiate structure of the ecto-plasin and ingested cells.

In sections from lesions slightly more advanced and

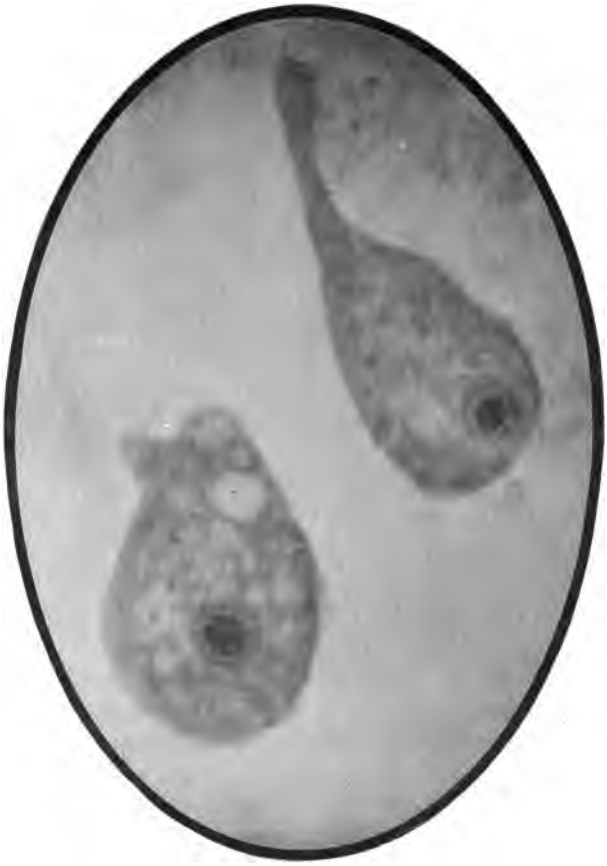

Fig. 26.—Amebas from a culture. Impression preparation. Borrel's stain. x 1,400.

showing a more extensive, though still superficial, necrosis, the glands immediately surrounding the lesions are hypertrophied and the cells show mucoid degeneration. There is the same lymphoid infiltration, with, if anything, a greater congestion. In the congested area each

gland mouth seems to be surrounded by a zone of hemorrhages. The cells of the necrotic mucous membrane are incorporated, with occasional leucocytes, granular detritus, amebas and bacteria, into a more or less well-formed membrane. There is a more extensive separation of the glandular cells, and in such glands amebas usually can be seen either in the lumina or between the cells and the basement membrane. Within the interglandular connective tissue amebas may also be seen in the blood vessels and lymph spaces. As the process progresses and as the lesions become more advanced, the effect on the submucosa is more marked. The congestion is augmented, the edema is increased and the number of amebas is greater. There is usually also an increase in the mucoid changes of the epithelium surrounding the lesion. On the contrary, in a few cases we have seen a very low, atrophic mucous membrane and a comparatively thin-walled gut, although there were extensive ulcerations. It is reasonable to suppose that we were dealing in such cases with an infection of a bowel previously the seat of a chronic enteritis. In all the cases that we have studied, regardless of the state of the mucous membrane or submucosa, we have seen an extensive lymphoid cell infiltration and at least a moderate hypertrophy of the lymphoid apparatus.

In all lesions, whether early or late, the character of the cellular infiltration is the same in uncomplicated cases. It seems, if amebas can be demonstrated in the tissues and if at the same time there is a polymorphonuclear infiltration, that bacteria are playing an active part in the process, especially if with the infiltration there is any degree of nuclear fragmentation. In certain cases, infiltration with polymorphous leucocytes may be seen about the margins of the ulcers, although at the base of the lesions and in the submucosa they were present in but inconsiderable numbers. In some cases, although there were some, or even many, bacteria present, there was no process that seemed to be directly attrib-

utable to these. It is possible that in such cases these were simply the non-pathogenic, harmless commensals of the amebas. In others, bacteria seemed to play at least as important a rôle as the amebas, noticeably in those cases in which there was diphtheritis and gangrene. It may be that the bacteria play an important part in determining whether or not hemorrhages shall occur, for it is certain that in uncomplicated cases thrombosis is a common and early occurrence. In many very early cases the interglandular vessels of the submucosa may be seen generally thrombosed. If an ulcer is filled with a diphtheritic slough which is carried away suddenly, the chances of the hemorrhages are much increased, as is the case in typhoid.

Usually the necrotic process extends for some distance beyond the ulceration and often beyond the amebas, but in many instances amebas seem to be present in healthy tissue, notably in the early lesions. It is a question whether this necrobiosis is the result of some secretion of amebas or whether it depends more on thrombosis. In some places one seems to be the predominating factor, in others the other, while in still others neither appears to be such. It is certain, however, that the thrombosis assists the amebas in extending their zone of action, as it may likewise assist the bacteria.

Necessarily the contents of the ulcers vary according to the degree of ulceration and to the character of the bacteria present. In uncomplicated cases, which microscopically show a rather clear, yellowish, gelatinous material in the opening, the ulcer contents are composed of a granular base of albuminous character, in which cells in various stages of degeneration are imbedded, together with amebas, bacteria and usually a few red blood corpuscles.

In all the lesions the amebas vary widely in size. Measured with a Zeiss-Scheiben micrometer, they range between 4 and 35 microns.

In the earlier stages of the amebic invasion, the edema affects the submucosa. In the later ones, the subperitoneal coat is also involved and adds considerably to the thickness of the gut. Eosinophiles are not uncommon in either the modified or unmodified amebic process. They occur, for the most part, in tissues at some distance from the lesions, usually in the neighborhood of blood vessels, and are not uncommonly encountered in the subperitoneal connective tissue when that layer has become edematous. These are, perhaps, more numerous in the secondary infections, as are also mast cells. Plasma cells are frequently seen in the submucosa. In the most extensive ulcerations the picture is modified only by the extent of the process. Whether the ulcers are undermined or not, there is always the same appearance of coagulative necrosis, with lymphoid infiltration, congestion and thrombosis, and comparatively little leucocytic invasion.

The two most evident features of the intestinal lesions, when viewed with a comparatively low power of the microscope, are the necrobiosis and the relative infrequence of leucocytes, features which suggest the important rôle of the amebas, for ordinarily in bacterial infection there is an associated local leucocytosis of varying intensity. A point of some importance is brought out by the fact that in the very early lesions—the preulcerative stage—the amebas may be encountered not merely in the glands, but beneath the epithelium and within the lymph spaces and blood vessels of the interglandular tissue and the submucosa.

THE CHARACTER OF AMEBAS IN SECTIONS.

In toluidin blue and eosin the ectosarc stains fairly definitely and the vacuoles of the protoplasm show well. The bacteria also stain, as do the encysted bodies and fragments. The nucleus is very definitely stained and surrounded by a more or less distinct perinuclear space. The nuclear membrane is a clear deep blue. The nu-

clear protoplasm is pink and contains one or several deep blue-black bodies, or perhaps none. There may be several dark-stained thickenings in the nuclear membrane. As a rule, in well-stained sections the amebas, where they do not contain much extraneous material, such as bacteria and nuclear detritus, are less deeply stained than the cells of the intestinal mucous membrane. The protoplasm of those deep in the tissues is less intensely stained than that of those in the mucous membrane, and it may be that this phenomenon is due to the fact that in the more superficial layers the organisms have taken up more mucous material. That there is some reason for this supposition is shown by the fact that this stain is much less useful in studying the organisms in liver abscesses, where, of course, there is no mucus.

Perhaps the most brilliant stain for amebas in tissues is that of Borrel. This consists of:

1. Saturated aqueous solution of Magenta red.
2. Saturated aqueous solution of picric acid. Saturated aqueous solution of indigo carmin aa.

Stain with No. 1 for 20 minutes and wash.

Stain with No. 2 for 5 minutes, wash and differentiate with alcohol, xylol and balsam.

With this the amebas are not so readily distinguished by the low powers of the microscope as with the thionin or eosin toluidin-blue stain, but the finer organization is much more easily studied with high powers. Generally, with this stain the amebas are less deeply colored than the surrounding tissues, being a rather pale bluish or purple, or, in well decolorized specimens, of a greenish hue. The edge of the organisms shows as a fine blue line, which is more distinct about the body of the parasite and less distinct about the pseudopodia. The ectoplasm appears as a finely reticular or almost hyaline substance, the fibrillar or granular part of which is stained a very faint blue. The endosarc appears as a granular material more deeply stained than the ectosarc, and purplish, bluish or greenish, according to the de-

gree of decolorization. Within this are spaces which remain uncolored, though in thick sections they have a bluish tint due to the underlying stained material. There may be bacteria also in the endosarc. There are also the rods of which Councilman and Lafleur speak, which are not seen in all cases, occurring in those in which there is more extensive sloughing or diphtheritis. It may be that these are crystalline, derived from the blood, or Charcot-Leyden crystals, which are occasionally found in leucocytes in certain conditions, and which Askanazy[6] says are oxyphilic.

The nucleus may be surrounded entirely or in part by a clear perinuclear space. The general color of the nucleus is violet or purplish. The outlines are sharp, and, if the section is not too decolorized, should be a clear crimson, which may be in the form of a complete ring or of an incomplete one, or may be nodulated on its inner surface, corresponding to thickenings in the chromatin. There are also occasionally crimson granules within the nucleus and occasionally one perfectly round mass corresponding to the nucleolus.

Ingested cells, such as red blood corpuscles, leucocytes, etc., may also be seen within the protoplasm in various stages of degeneration, the stain depending on the extent of the process.

In sections so decolorized that the magenta is all removed, the nucleus appears a blue color deeper than the tint of the rest of the cell and with the chromatin material still more deeply stained.

Heidenhain's iron hematoxylin is as excellent a stain for amebas as it is for other tissues, although not so brilliant as the magenta-picro-indigo carmin. In carefully manipulated sections the nucleus of the amebas is somewhat more deeply stained than the cystoplasm and ordinarily appears as a dense blue-black ring, in the center of which is the round black nucleolus. The nuclear plasma is usually just of a blue tint and is di-

6. Munch. med. Wochft., 1904, vol. li, 1945.

vided by a mesh of delicate dark reticulum. There may be other deeply stained chromatic elements or granules within this. The radial striæ of the cytoplasm is well shown and the crystalline bodies are, when present, an intense black. The spongioplasm appears as a network of dark lines and the cell boundary is sharply differentiated. Red cells, when present, stain according to the state of degeneration, those most recently ingested being black, those least recently yellowish. Bacteria, when present, stain sharply and distinctly, when not too far degenerated or digested.

Amebas grown in cultures from amebic ulcers, when stained by Borrel's method, show somewhat different staining reactions.

Cover-glass impressions may be made in the following way:

A cover-glass is placed on the growths on agar plates, removed quickly and instantly plunged into a very hot saturated solution of mercuric bichlorid. They are then washed in Gram's solution or a weak tincture of iodin, and rinsed in 80 per cent. alcohol, after which they are washed in water. The stain is then applied in the usual way. After this process the preparations are differentiated in alcohol, cleared in xylol and mounted in xylol-damar. The amebas are seen in various conditions, as they were in the culture, and of various shapes and sizes. In many the pseudopodia have not been withdrawn and can be well seen. Under these circumstances the ectosarc has a pale, diffuse, blue color, or is perhaps very finely granular and has a very sharply differentiated limiting line. Usually, however, this is not well seen and the whole organism has a sharply circumscribed, blue, granular appearance. The contractile vacuole shows clearly as an unstained, ovoid or oval space, usually near the surface of the organism, but occasionally near the nucleus.

The nucleus is composed of a round, central, deep purple body, surrounded by a narrow, pale bluish,

homogeneous zone, and this, in turn, is surrounded by a denser, blue, granular zone. About this, in turn, is ordinarily a second more or less faintly stained zone. The whole nuclear body is round or slightly oval. The nucleolus is always round.

Comparing the amebas in such preparations with those in sections, we can readily see that the relative size of the nucleus is the same, as is also the relation between the protoplasm and nucleus; but in the tissues the contractile vacuole is usually not so distinct and the nucleus does not present the same appearance. This may be due to the fixation or it may be due to the different degree of decolorization. The dissimilar nutritive conditions may also affect the microchemical staining reactions.

The small amebas, those the size of an erythrocyte or smaller, should show the same relation in the size of nucleus and cell body.

The distinguishing feature of the amebas is their generally irregular or oval shape, though they are often round, their relatively small, round nucleus, and the larger amount of granular or vacuolated protoplasm, which often contains foreign bodies.

RELATION OF THE AMEBAS TO THE TISSUES.

The Mucous Membrane.—It is not known whether the amebas are able to attack or to pass through an intact mucous membrane; in fact, it seems probable that in order for them to enter the deeper layers of the intestine there is some change from the normal (Schaudin). It is possible that catarrhal conditions, however slight, are accompanied by erosion, or necrosis of even a few, of the superficial cells, and would offer the necessary conditions for invasion. It is, at any rate, certain that the amebas have less influence on the epithelial cells than on the supporting tissue. That this is true may be demonstrated repeatedly. In many glands the amebas may be seen either in the lumen or between

the lining cells and the basement membrane. As a rule in these cases the epithelium detached has lost no more of its normal character than might be expected, and if adherent it seems more healthy than would be imagined in the presence of an organism whose power of causing cellular destruction is as great as it is in the case of the ameba. Generally speaking, epithelium seems to have as great resistance to the ameba as has muscular tissue.

Muscle.—In all works on amebiasis attention has been called to the lack of resistance the connective tissue offers to the progress of the organisms. Attention has been repeatedly called to the fact that the extensive ulcerations are in form and situation dependent on this quality in the submucous layer of the intestinal wall. The preliminary feature of the changes in this position is edema, which, after invasion by the amebas, is followed by swelling of the fibers and cells, infiltration with round cells and lymphocytes, sometimes accompanied by fibrin formation. The nuclei of the swollen cells become paler, the appearance of fibrillation is lost and the tissue becomes hyaline or necrobiotic. A further feature of the process is that new tissue is found early and this has the appearance of granulation tissue. Suppuration, as previously indicated, probably does not occur in the uncomplicated disease.

Blood Vessels.—Just how the organisms enter the blood vessels can not be satisfactorily stated. In some sections they are seen in these vessels in large numbers, in the same or others they may be seen in the perivascular lymph spaces or they may appear immediately beside the endothelium of the capillaries. It is possible that they enter directly through the capillary walls by virtue of their inherent power of progression, in much the same way as the leucocytes wander in and out. There is the possibility that in the process of tissue destruction the vessel walls are so changed as to make this process more practicable, or that following

capillary hemorrhages and before coagulation had occurred the organisms may enter the vessels and make their way along. Certain it is that they do not necessarily cause thrombosis by their presence, although this appearance is by no means uncommon in tissues, and especially in the vessels of the interglandular tissues. So far as the blood cells are concerned, the amebas are able to ingest and to destroy apparently healthy erythrocytes and leucocytes.

Cells.—It was shown by Councilman and Lafleur, and forcibly insisted on by Howard, that leucocytic infiltration is not a feature of amebiasis. On the contrary, it is stated that the process is more in the nature of a subacute or chronic inflammation, in that the cells predominating in the infiltration are formative ones and lymphocytes. In addition to these last mentioned cells there is often a considerable number of eosinophiles, though this is not the rule. If the condition is a chronic inflammatory one, however, then this is the type of infiltration we should expect, for lymphocytes and eosinophiles are the cells which, par excellence, occur in such pathologic states.[7]

In one series of sections we saw considerable numbers of mast cells, which occurred chiefly in the glandular layer of the bowel. On what conditions the presence of these depends we can not say, except to note that in the bowel from which the sections were made there was considerable diphtheritis.

Plasma cells are not uncommonly seen in the submucosa, as Councilman and Lafleur state. If these cells are of lymphoid origin, we should expect them to be frequently met in subacute or chronic inflammation in which there is a proliferation of, and invasion with, lymphoid cells.

RELATION OF AMEBIAS TO BACTERIA.

From our experience it can not be said that the pres-

7. Muir. Brit. Med. Jour., 1904, II, 585.

ence of bacteria limit the field of activity of the amebas. As a matter of fact the organisms seem to be about as numerous in cases complicated by bacterial superinfections as in uncomplicated ones, unless it be in those in which pyogenic cocci are present. In one case so complicated there were certainly fewer amebas in the lesions and there was very active leucocytic infiltration with marked coincident karyorhexis, a very uncommon picture for amebiasis.

When amebas are found in exudates rich in bacteria they show evidence within their bodies of a very active phagocytosis.

CONCLUSIONS.

1. Intestinal amebiasis is a peculiar ulcerative condition of the intestine caused by Amœba coli (Lösch) usually confined to the large intestine, though occasionally (7 in 200 cases) the ileum is affected and more often (14 in 200 cases) the appendix is involved.

2. In the majority of cases the condition affects the entire bowel (159 in 200 cases), though it may be limited to one or more portions, most commonly the cecum and ascending colon (23 in 200 cases).

3. The ulcers show a tendency to be undermined, due to the lack of resistance on the part of the submucous layer of the bowel.

4. The organisms may enter the blood vessels very early in the disease and may be transported to the submucosa without lesions of the muscularis mucosa.

5. The disease is a subacute chronic inflammatory process, as shown by the character of the exudate and infiltration, by the early formation of granulation tissue and by the absence of leucocytic infiltration.

6. Complete healing may be accomplished, or a condition of chronic atrophic enteritis or chronic catarrh may persist, which is known as sprue or psilosis.

The photographs and photomicrographs were made by the Government Photographer, Mr. Martin. The

colored drawing (27) was done by Dr. W. B. Wherry. The other colored drawings were made by Mr. Espinosa, the artist of the Bureau of Government Laboratories. To these gentlemen we take occasion to express our thanks.

DISCUSSION.

Dr. George Dock, Ann Arbor, Mich., said in regard to the importance of distinguishing the latent, that he was fortunate enough to see a latent, mild or variable case very long ago, and he has already called attention to it. Briefly, the history of the case is as follows: The patient was a man who, for several months, had no loose stools at all and no diarrhea, and was absolutely free from any symptoms ordinarily referred to as dysenteric, yet he developed a liver abscess which was operated on and proved to be amebic. The patient died a few days later, and it was shown that not only were there lesions in the cecum, but also in the upper part of the large intestine, as well as in the liver. The stools Dr. Dock examined and found no amebas or other evidences of the disease. If the patient had been under his observation a longer time the diagnosis might have been made prior to death, especially if saline cathartics, as Carlsbad salts, had been given to facilitate the examination of the stools. In diagnosis, the most important thing is the proper examination of the stools, and this has been much neglected because it has been supposed to be so difficult. By giving Carlsbad salts, stools can be secured whenever wanted, and there is really no difficulty in finding the amebas, even in cool media or in cool rooms. As an important and practical aid in this examination of the stools, they should be examined, not in deep vessels, but in flat vessels, the broad low granite dishes answering the purpose very well. A certain amount of practice is necessary in order to be sure always that what is seen are really amebas. Dr. Dock likes the modification of Jenner's stain, which he believes to be as good as the specific stains. His experience in the South shows that it is comparatively easy to treat this disease if it is seen at the beginning. Cathartics should be vigorously given, and irrigations of any kind are useful, his preference being for strong saline solutions. In the chronic cases the treatment is more difficult. These latent cases are the ones which are likely to be seen in this country. At the Saratoga session, Dr. Dock was able to report such a case, and within the last year he has seen another example which occurred in a man who had never been outside of the United States at all, and yet he had a severe infection with *Amœba coli*. The greatest care possible is demanded in the treatment of the patient. It is very necessary that constipation should be avoided. Instructions regarding the diet may vary greatly.

He has seen beneficial effects from the use of ipecac used after the manner of Strong, covering it with salol. About one year ago he saw an interesting case of amebic infection from the Philippine Islands. The patient had amebic dysentery, as well as uncinariasis and the *Tricocephalus dispar.* He was treated for uncinariasis with thymol, and the amebic signs then disappeared as well. Although this is spoken of as a tropical disease, it may occur in other parts of the country. Though the clinical picture varies greatly, the diagnosis can be made, and the treatment is becoming more and more satisfactory.

Dr. H. R. Lemen, Alton, Ill., stated that he has had two years' experience in the Philippines, and made careful examinations of 532 males and 53 females who were taken there as prisoners without any apparent evidences of the disease whatever, and he found 91 males and 11 females with amebas. Among 50 soldiers there were found 10 cases of liver abscess.

Dr. Stanley Black, Los Angeles, Cal., asked Dr. Musgrave for the points in differential diagnosis between *Amœba coli* and other amebas which exist in the stools. Dr. Black has seen a number of cases in which amebas were present in the stools, but in which there were no symptoms of dysentery, such as one expects to find when the *Amœba coli* is present. He also asked if Dr. Musgrave considers the presence of red corpuscles diagnostic of the *Amœba coli* and if the pathogenicity for cats is of importance in diagnosis. In Dr. Black's opinion the material for examination can best be obtained by the introduction of a rectal tube. The mucus so obtained often contains many amebas.

Dr. F. C. Shattuck, Boston, stated that he has seen one case of amebic dysentery in a man who had not been out of New England. This simply corroborates what has already been stated, that the disease is not necessarily one of the tropics.

Dr. Claude A. Smith, Atlanta, Ga., said that physicians meet some cases of amebiasis in the South, but of course not anything like the number found in Manila. As an illustration of the fact that some patients appear to recover or even recover without treatment, Dr. Smith said that five years ago, at the request of Dr. H. F. Harris, he made a postmortem examination of a man who ten years previously presented clinical symptoms of a severe type of the disease. He removed the colon, but there was no evidence of any ulceration, nor any macroscopic signs of previous ulceration. This also showed that the symptoms of the patient are not necessarily an index of the extent of the lesions. He recalled one or two autopsies in which he found extensive ulcerations throughout the colon, and yet the clinical symptoms did not indicate anything serious. There was one case in a negro man, about 45 years of age, whose muscular development was perfect, presenting no signs of emaciation, and who was not

considered to be in serious condition, and yet he died forty-eight hours after admission to the hospital. The colon's entire mucous membrane was found to be necrotic, and yet that man had been hard at work until two days before death. He asked if Dr. Musgrave has been able to trace these cases of amebiasis after apparent recovery, and if he has found many relapses.

Dr. W. E. Musgrave, Manila, P. I., said that all the questions and points brought out in the discussion have been carefully gone over in the present paper and in previous publications. (See The Journal A. M. A., April 8, 1905, p. 1098, and Bull. 18, Bureau Government Laboratories, Manila.) In conclusion he emphasized the fact that the symptoms produced by this affection are in no way proportionate to the danger done to the bowel.

FURTHER REMARKS ON THE MODE OF INFECTION IN UNCINARIASIS.

CLAUDE A. SMITH, M.D.

Pathologist to Grady Hospital, Baptist Tabernacle Infirmary, Professor of Pathology and Bacteriology, Southern Dental College; Demonstrator of Pathology, Atlanta College of Physicians and Surgeons; Secretary Anatomical Board of Georgia.

ATLANTA, GA.

At the session of this Association at Atlantic City last year I presented a report of an experiment on a human being to determine whether the larvæ of the uncinaria would penetrate the skin. At that time I reported that, after placing soil containing larvæ on the skin of an individual, an eruption had followed, and that, after a period of seven weeks, the eggs of the uncinaria were found in the feces.

In this paper I report a second experiment, similar to the first, in which the soil containing the larvæ was placed on the wrist of an individual who had shortly before been discharged from the hospital after an operation for hernia, and the eggs of the uncinaria were found in the feces during the sixth week afterward.

In the first case, it was not feasible to obtain photographs of the various stages of the eruption produced on the skin by the larvæ, but in this second case I was able to do this, and present them in the report which follows:

METHOD OF PROCEDURE.

Preliminary Arrangements.—After making arrangements with the patient regarding the experiment, a specimen of feces was obtained containing an abundance of the eggs of the uncinaria. Some soil was next ob-

tained and baked for an hour so as to eliminate any other organism. After cooling this soil, the feces containing the eggs were then mixed with it until the odor of the feces had about disappeared, sufficient water being added to render the mass slightly damp. This mixture was then placed in Petri dishes and kept at the room temperature.

At the end of twenty-four hours an examination of the soil showed that the eggs had all hatched out, as no eggs could be found, but there was an abundance of the young larvæ.

Fig. 1.—The soil containing the larvæ as it appeared on the wrist, the tendons and veins of the hand showing distinctly.

Application to Skin.—An important point to be determined was the age at which the larvæ would penetrate the skin. It was decided, therefore, to place the larvæ on the skin every day from the time they were twenty-four hours old until some result was obtained. Accordingly when these larvæ were twenty-four hours old some of the soil was placed on the wrist, wrapped with a plain gauze bandage and allowed to remain for one hour. At the end of this time the soil was removed and the wrist examined. No effect was apparent and the patient said he had experienced no sensation during the period.

This procedure was repeated when the larvæ were forty-eight hours old, and again on the third, fourth and fifth days. No result whatever was obtained, and this was rather surprising, as the results in the previous experiment were obtained when the larvæ were four days old.

On the sixth and seventh days the patient failed to appear, but he reappeared on the eighth day, and the soil was again bound on the wrist and allowed to remain for one hour.

Within five minutes after the soil was placed on the

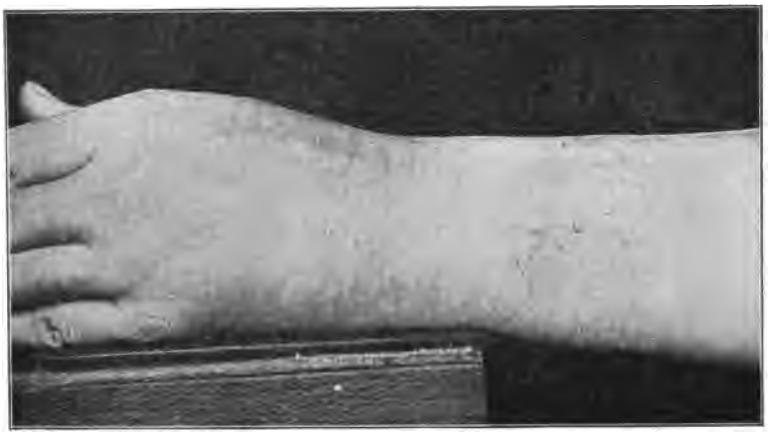

Fig. 2.—Showing swelling of wrist, obliterating veins and tendons of hand and vesicle formation.

wrist the patient complained of a sharp, stinging sensation in the area covered by the soil, which increased and persisted during the time the soil was allowed to remain on the wrist. At no time was the wrist of the patient given any treatment whatever before applying the soil. The soil was simply placed directly on the skin as shown in Figure 1. (About the third day a simple ointment was placed on the eruption to relieve the anxiety of the patient.)

Treatment of Wrist.—After remaining on the wrist for one hour the soil was removed, and on inspection

the entire area was found to be decidedly reddened. The soil was thoroughly removed and the wrist was then carefully wrapped with a number of layers of plain gauze bandage, and the patient was instructed not to remove this and to return the following day.

On coming back the next day, the patient said that the stinging sensation had gradually subsided the day previous, but that during the night the intense itching of the area was so annoying as to interfere with his sleep. On removing the bandage from the wrist the

Fig. 3.—Showing the large crust forming over the area and the decrease of the swelling.

redness over the area was increased, the area was slightly elevated, and the entire dorsum of the wrist was swollen. The patient was instructed to restrain any desire to scratch the area, but to be sure that the area would not be damaged by the finger nails of the patient while asleep the layers of gauze bandage were replaced.

Constitutional and Local Symptoms.—On returning the day following, the patient stated that he had slept scarcely any at all the night before on account of the excruciating itching, and that he had rolled and tossed all night.

Removal of the bandage showed the wrist greatly swollen, the swelling extending downward over the back of the hand and upward a short distance on the forearm. The area which had been covered by the soil was intensely reddened, and vesicles covered the entire area. On direct pressure, however, the patient said that there was very little tenderness. The lack of tenderness was a marked feature throughout the course of the eruption. This was true in the first case. The condition of the wrist at this time is shown in Figure 2.

On the third day of the eruption, the swelling had extended down over the first phalanx of the fingers and upward to about half way to the elbow. The swelling

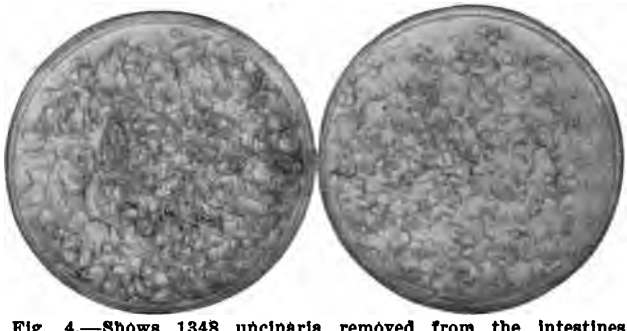

Fig. 4.—Shows 1348 uncinaria removed from the intestines twelve weeks after the eruption on the wrist.

reached its height at this time. The vesicle had become confluent, forming large blebs, and the redness was more intense. The itching was still severe, but the patient said he had rested better than on the two previous nights. There was some redness up the inner side of the forearm, but no involvement of the axillary glands.

On the fourth day, some of the vesicles had ruptured, moistening the bandage, and the swelling had begun to recede. The patient had rested much better than previously. The itching had also decreased in severity.

On the fifth day, many of the vesicles had ruptured, and a crust had formed over a part of the area. The swelling had greatly decreased, the veins and tendons

showing well through the skin. Previously they had been obliterated by the swelling. The patient now said he was feeling all right again. Figure 3 shows the hand at this time.

On the sixth day, almost the entire area was covered by the crust which had formed, only a few vesicles remaining. Only a trace of the swelling remained about the wrist, and the patient said that the slight itching sensation which remained was not confined to the area of the eruption, but was scattered over the entire forearm.

On the eighth day, the crusts which had formed over the area had begun to scale off, the swelling was practically all gone, and the patient said that he felt about normal again.

Examination of Feces.—The feces of this patient were carefully examined at the beginning of this experiment, the feces being washed and centrifugated, as by this method I have found that it is possible to detect the slightest infection with uncinaria, but no eggs of the uncinaria were found. After beginning the experiment, the feces were examined twice a week, but with negative results until the middle of the sixth week after the soil was placed on the wrist. At this time a few of the eggs of the uncinaria were found in the feces, and after this they steadily increased in number.

As this patient was just out of the hospital after an operation, no examination of the blood was made, as under the circumstances this was considered to be of such uncertain value as not to be worth while.

Soon after the appearance of the eggs in the feces, in reply to questions, the patient said that his bowels were inclined to be loose, and a week or so later this had increased to a mild diarrhea. This cleared up in a week or so more, and the patient said his stools were normal.

Eight weeks after the appearance of the eggs of the uncinaria in the feces of the patient, he was given the usual treatment to remove the parasite, i. e., two doses

of thymol of 30 grains each, preceded and followed by a large dose of salts. All the stools were saved for twenty-four hours following the treatment, and these were carefully washed and examined. As a result, 596 adult male uncinaria and 752 female uncinaria were found, making a total of 1,348.

Some time after this the feces of the patient were again examined and found still to contain a few eggs of the uncinaria. Since then he has been given the treatment at two different times, but at the present time still has a slight infection.

SUMMARY.

In the criticisms of the experiments of Looss, Pieri, the assistant of Grassi,[1] states that the experiments of Looss are uncertain, because Looss can not be sure that the infection in his case was not through the mouth on account of his having handled the larvæ so much.

In this last experiment performed by me, I took great pains to be sure that the patient could not come in contact with the larvæ at any other time than when placed on the wrist by me, and the fact that such an enormous number were found in the intestines would discredit any idea that the infection was through the mouth, as mentioned by Pieri.

The deductions from these experiments, I think, are plain. That the disease is contracted through the skin is supported by the clinical observations which I have reported previously. That this is the only way in which the disease is contracted I am not sure, but it appears to be the mode of infection in the great majority of instances.

These experiments also show that the eruption has no tendency to spread when it is not disturbed by scratching and has a duration of only a few days. When the eruption occurs under natural conditions, however, the individual scratches and tears the eruption, infecting

1. Centralb. f. Bakteriol. und Parasit., Erste Abteilung, xxxiv, 1903, 531, and Arch. Italiennes de Biologie, xxxvii, 1902, 269,273.

the entire area and spreading the infection over a large additional area, and as a result of this the eruption is often weeks in healing up.

A study of the climatic conditions I find to be of value in determining just when and under what conditions these larvæ penetrate the skin in the natural conditions. These observations have not yet been completed. I hope to be able to report on them later.

Last year I reported some examinations of tissue which had been subjected to the larvæ, but in which I had not been able to locate the larvæ. These experiments I have not had an opportunity to repeat, and, therefore, they are still uncompleted.

DISCUSSION.

Dr. Richard C. Cabot, Boston, said that two great medical achievements have resulted from the war with Spain. We have freed Cuba of yellow fever and we are now freeing Porto Rico from uncinariasis. To Capt. Baily K. Ashford, U. S. A., and Lieut. W. W. King, U. S. P. H. and M. H. S., we owe much of what has been done. They have conducted a field campaign against the disease among the whole people of Porto Rico. They have field hospitals, tents, etc., which they take from town to town; they camp outside the towns and there they treat the population. The people come down to them to be treated. When they have intense anemias to deal with the patients are treated in bed, while those with milder cases take the medicine given them and go home. Every case is diagnosed by means of the microscope, the stools and blood being carefully studied. Two American physicians have organized and pushed a plan to treat practically the entire population of Porto Rico. Dr. Ashford and Dr. King are engaged in this work now, as they have been for a number of months. They were invited to be present at this meeting, but they were detained in the service, and are even now engaged in their splendid work. They ask nothing from us, but their fine service certainly demands from us knowledge of the work and our sympathy. The results have been published in brief, but not in detail in the journals, and are known less widely than they deserve. Dr. Cabot looks on their achievements as destined to be as beneficent as the work of Reed and Carrol on yellow fever in Cuba.

Dr. M. H. Fussell, Philadelphia, asked if Dr. Smith considers the ground itch as the only source of this parasite in the human being, or if the affection may occur by the parasite being swallowed, and whether he has any idea or made any calculations of how many embryos there may have been in

the mass that he placed on the patient's wrist. Dr. Fussell understands that the embryo or parasite does not increase in the intestines of the individual. He said that he would also like to know if the blood was examined and the eosinophiles counted.

Dr. Philip King Brown, San Francisco, stated that in San Francisco physicians have experiences with three classes of uncinariasis. The first class came from Mexico, evidently a pure class. Then came soldiers, returning from the Philippines, without having had any symptoms of uncinariasis before discharge. Some of them were kept in the general hospital with amebic infection, and were discharged, but nothing was known regarding the presence of uncinariasis. Many of these cases came to the county hospital. A peculiar thing about some of these soldiers was the striking symptoms that occurred when there were few parasites. Dr. Brown recalled one patient who came near dying of anemia and yet the physicians could find but seven parasites. The third class of cases was found among the Porto Ricans who were sent to the Hawaiian Islands to replace Japanese laborers on sugar plantations. They were not a success, and were returned to San Francisco, where a large majority of them still remain. They present the type of the disease which has been so thoroughly investigated by Ashford. Attempts have been made by Gunn of San Francisco, who has studied the cases in San Francisco very thoroughly, to find the parasite in infants born since these Porto Ricans left their native home, but thus far they have not been successful. He has, however, discovered several cases of bilharzia infection in these Porto Ricans.

Dr. Claude A. Smith, Atlanta, Ga., in reply to the questions stated that, while he can not say that the passage of the parasite through the skin is the only way by which it gains access to the human body, yet from the experiments and from the clinical history of the cases this mode of access appears to be the rule and the ingestion through the alimentary canal the exception. In growing the larvæ in the laboratory, it was noticed that they would climb on the sides of the vessel. This would cause us to suspect that they would climb on plants from their natural development in the soil, and if so, it is possible that they might be swallowed by persons eating raw vegetables. He said that it was impossible to count the number of larvæ contained in the soil which he placed on the wrist of the patient. They were intensely concentrated, more concentrated than they would ever develop under natural conditions. There were undoubtedly many thousands in the small amount of soil which he used, as examination under the microscope showed it to be swarming with them. Autoinfection, he said, is practically an impossibility. His experiments indicate that the larvæ will not attempt

to enter the tissues before they are four or six days old, and it is not likely that the eggs would remain in the intestines for this length of time, even if they could find conditions suitable for hatching. As before stated, no blood examinations were made in this case, as the patient was just out of the hospital, and such examinations, therefore, would have been of uncertain value. Dr. Smith inclines to the view that the parasites pass into the veins and thus get into the circulation. In the experiments the inflammation of the forearms above the eruption appeared more as a phlebitis than a lymphangitis. The children of all classes in the South go barefoot in the summer, and all are subject to the ground itch, but it is most common among the poorer classes in the country. As the better classes are less exposed to the disease, they usually have a mild form which can only be diagnosed by the examination of the feces, and as there are no objective or subjective symptoms these cases are generally overlooked. It is only the severe cases which interfere with the development of the person and which present symptoms of the disease. Those individuals who have had only one or two attacks of ground itch have only a small number of the parasites in the intestines, and these produce no effect on the development of the person. It is only when there have been a number of attacks of ground itch (usually covering a period of several years) that there is any interference with the development of the body. A study of the climatic conditions shows that in many sections the conditions favorable to the development of the parasite occur only two or three times during a summer. When the conditions are favorable for the development of the parasite one will usually find every child of an entire family infected, but usually there is not more than one who has the severe type of the disease. In the majority of the cases of the severe type of the disease, the patient will eventually "outgrow" the disease; that is, the child will begin wearing shoes at 15 or 17 years of age, and from that time on the parasites gradually die out.

OFFICIAL MINUTES.

TUESDAY, JULY 11.—AFTERNOON.

Dr. Richard C. Cabot in the Chair.

"The Incidence of Heart Disease in San Francisco," by Dr. William Fitch Cheney, San Francisco. Discussed by Drs. Ophüls, Walsh, and Grandy.

"The Nostrum Evil," by Dr. Frank Billings, Chicago. Discussed by Drs. Musser, Moore, Stengel, Walsh, Bridge, Priestley, Witherspoon, King, Grosse, McCleave, Stockton, Stengel, Bridge, and Carter.

"The Effects of the Inhalation of the Fumes of Nitric Acid, with Report of Cases," by Drs. J. N. Hall and C. E. Cooper, Denver. Discussed by Drs. N. H. Neilson, Milwaukee, Wis.; John H. Musser, Philadelphia; G. W. McCaskey, Fort Wayne, Ind., and Dr. Hall.

"Studies in Roentgen Ray Diagnosis of Chest Diseases," by Drs. James E. Talley and W. S. Newcomet of Philadelphia (read by Dr. Hall). Discussed by Drs. Neilsen, Musser, McCaskey, and Hall.

Dr. Alfred Stengel, Philadelphia, offered resolutions, which, on motion, were referred to the House of Delegates. (These were approved and are printed in full in THE JOURNAL, July 22, 1905, page 275.)

WEDNESDAY, JULY 12.—MORNING.

SYMPOSIUM ON NEPHRITIS.

A paper on "General Considerations on the Pathology of the Kidney," by Dr. W. T. Councilman, Boston, was not read, but reference was made to it by the Chairman, Dr. Cabot.

"Albuminuria in Nephritis and Bright's Disease," by Dr. Alfred Stengel, Philadelphia.

"Cylindruria," by Dr. Charles P. Emerson, Baltimore.

"The Relation of Kidney Conditions to Puerperal Eclampsia," by Dr. Philip King Brown, San Francisco.

"The Dietetic Treatment of Nephritis," by Dr. F. C. Shattuck, Boston.

These five papers were discussed by Drs. Witherspoon, Ophüls, Bulkley, Hutchinson, Francine, Walsh, Billings, Musser, Fussell, Le Roy, Lichty, Stengel, and Brown.

WEDNESDAY, JULY 12.—AFTERNOON.

SYMPOSIUM ON ANIMAL PARASITES AND TROPICAL DISEASES.

"Symptoms, Diagnosis and Prognosis of Amebiasis in the Tropics," was read by Dr. W. E. Musgrave, Manila, P. I., with abstract also of a paper on "The Pathology of Amebiasis," by Drs. Paul G. Woolley and W. E. Musgrave. Discussed by Drs. Dock, Lemon, Black, Shattuck, Smith, and Musgrave.

"The Mode of Infection in Uncinariasis," by Dr. Claude A. Smith, Atlanta, Ga. Discussed by Drs. Fussell, Cheney, Brown, and Smith.

A nominating committee was appointed, consisting of Drs. Hall, Stockton and Shattuck.

THURSDAY, JULY 13.—MORNING.

SYMPOSIUM ON THE STOMACH.

"Recent Advances in the Physiology of Human Nutrition," by Dr. Frank Billings, Chicago.

"Methods, Value and Limitations of the Knowledge of the Gastric Contents," by Dr. George Dock, Ann Arbor, Mich.

"Non-Gastric Diseases Presenting Gastric Symptoms," by Dr. J. H. Musser, Philadelphia.

"Food Stagnation from All Causes," by Dr. Charles G. Stockton, Buffalo, N. Y.

These four papers were discussed by Drs. Cabot, McCaskey, Manges, Black, Miller, Anders, Shattuck, Bond, Walsh, Lichty, Cooper, Bridge, Billings, Dock, Musser, and Stockton.

"Type of Tuberculosis on the North Pacific Coast" by Dr. Woods Hutchinson, Portland. Discussed by Drs. Cheney, Miller, Bridge, Brown, Ophüls, Robbins, Osborne, Moffit, and Hutchinson.

ELECTION OF OFFICERS.

The election resulted as follows: Chairman, Dr. Herbert C. Moffit, San Francisco; secretary, Dr. J. L. Miller, Chicago; alternate, Dr. George Dock, Ann Arbor.

"Coccidioidal Granuloma," by Dr. W. Ophüls, San Francisco. Discussed by Dr. Ryfkogel.

"Thyroid Disease in California," by Dr. Herbert C. Moffit, San Francisco. Discussed by Drs. Walsh, Wells, Quevil, McCaskey, Whiteside, Grandy, Lichty, Johnson, and Moffit.

"The Value of Various Hemoglobin Instruments to the General Practitioner," by Dr. M. Howard Fussell of Philadelphia.

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